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Medical News Letter

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MEDICAL NEWS LETTER

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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390 (Code 18), giving full name, rank, corps, old and new addresses, and zip code.

FRONT COVER: NAVAL MEDICAL RESEARCH UNIT NUMBER THREE. This research facility, the outgrowth of the American Typhus Commission created by President F.D. Roosevelt in 1942, was commissioned by the Navy in 1946. The Egyptian Government granted a 25-year lease to the United States for a 2½ acre tract of land for 23 cents a year, and NAMRU-3 was officially dedicated on 27 October 1948. Its mission is to conduct research in the Near and Middle East, Africa, Europe and India into diseases and medical problems important to military forces operating in tropical and semi-tropical regions. It also develops methods of preventing and treating parasitic and infectious diseases. Being centrally located and the only U.S. medical laboratory in Africa, the Unit deploys teams to Middle East areas where epidemics occur, and has the cooperation of Egyptian scientists. It has provided technical support and consultative services to European scientists, and has sent survey and task forces to countries in the Near East. In 1960 NAMRU-3 helped combat an epidemic of Kala Azar in the central Sudan and later conducted a classic ecological study of the disease. Areas of immediate scientific interest include Malta fever, malignant diseases, intestinal parasites, virus diseases, poliomyelitis, typhoid fever, typhus, dermatological disorders, and the clinical manifestations of dietary deficiency states. The Addis Ababa Detachment was opened in mid-1965 and has done important work on the role of mosquitoes in transmitting viruses, the role of bats and rodents as host-disseminators, and the occurrence of drug-resistant malaria in Ethiopia. The Unit is trying to control flies and mosquitoes in Egypt, and is doing research on ticks, fly-borne eye disease, and snail-borne diseases. Infant malnutrition and anemias associated with parasites are being studied. Notable contributions to public health have been made through research on cholera, arbor viruses, zoonoses, plagues, West Nile Fever and Sand Fly Fever. NAMRU-3 has gained an international reputation through its contributions to the knowledge and treatment of exotic diseases. Its activities at Cairo have survived many political changes.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

PREOPERATIVE PROPHYLAXIS OF POSTOPERATIVE PAIN

Charles W. Quimby, Jr., MD, LL.B, Med Clin N Amer 52(1):73–80, January 1968.*

Postoperative pain, and the drugs used to manage it, can initiate or perpetuate pulmonary, cardiovascular, gastrointestinal, and urinary tract complications. The purpose in outlining a preoperative program for the control of postoperative pain is to anticipate the complications of pain and its treatment, and to minimize or avoid them. Such a program assumes the patient will have to participate actively in his own care and his physicians will have the responsibility of teaching him how to participate effectively.

A complaint of pain can signify bodily damage, it may be a call for help, and at other times it may be for pleasure gratification through attempting to create a supportive relationship with another. It is precisely the last relationship that must be established before operation so that the patient's need for psychologic support and pain relief can be met postoperatively. This is an addition to, but not a substitute for, the rather impersonal postoperative care surgical patients usually receive.

The internist referring the patient for a surgical procedure has the first opportunity to initiate preoperative prophylaxis of postoperative pain. The surgeon has the next chance when he recommends the operation. The anesthesiologist must judge on his preanesthetic rounds the night before operation how effective his colleagues have been and be prepared to build upon the program they have begun. If they have failed to initiate one, the anesthesiologist has the last clear chance to start such a program in the traditionally short time accorded him.

Guidelines in Evaluation and Management

Rapport

While the internist, surgeon, or anesthesiologist is assessing the patient, the latter is making up his own mind about his doctors. Sapolsky has pointed out that when the patient believed his physician understood him, the therapeutic outcome was better than when the patient thought his physician did not understand him. More important, he showed that this mutual evaluation was an evolving process—not a one-interview affair. Hence, since the referring internist has usually established rapport, then the preoperative prophylaxis of postoperative pain ought to begin in his office. The next logical man to develop rapport with the patient should be the surgeon.

On the other hand, the anesthesiologist is in a different situation because of the short time usually accorded him to evolve a meaningful patient-physician relationship. When the anesthesiologist makes his preoperative rounds, he introduces himself to, interviews, and examines a patient who is in the throes of adjusting to the imminent anesthesia and operation. This crucial adjustment severely tests the patient's maturity and adjustment. In addition, the death and punishment symbolized by anesthesia, and the punishment, penetration, and mutilation implied by surgery, force the patient to fall back upon those defenses that have withstood the test of time. These were developed early and they may be imperfect and often inappropriate and immature. Hence the anesthesiologist is likely to be initiating a relationship with a patient who finds it difficult to relate and who is regressing or has regressed. Rapport may be difficult to establish but it must be developed if the anesthesiologist is to form a supportive relationship that looks to the postoperative period.

Impact on Self-Image

The physician must early determine the impact of the impending anesthetic experience on the patient's body- or self-image. Usually this is ignored and emphasis is placed on the impact of the operation and its consequent pain. But the impact of anesthesia is important. In 18 percent of Sheffer and Greifenstein's patients there was a nearly delu-

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sional belief that *general anesthesia* permanently altered body function by loss, perversion, or penetration. There was no explanation for this. Anesthesia, together with surgery and the associated pain, are an assault on the patient's body- and self-image as well as a physical assault. How the patient accepts these assaults varies. If the patient decides his body-image has been weakened, pervasive changes will occur in his personality and social identity concepts. We can predict that about 20 percent of patients submitting to operation have pervasive changes occurring in their personalities because of the above beliefs. The physician must anticipate these changes even though he will not be able to describe them in advance.

Pain

The second element for analysis is the patient's reaction to pain. In the long run the psychological reaction to pain and operation determines if and how well the patient will cooperate with postoperative therapeutic regimens. To plan a program for the preoperative prophylaxis of postoperative pain the physician must: (1) spell out in advance the site, intensity and duration of the pain the patient will experience after the operation; and (2) using the patient's own preoperative behavior as a guide, outline in general terms how he will react psychologically both to the operation and the postoperative pain.

The site and intensity of the patient's pain are easy to predict: The bone pain of the patient who has had a bunionectomy does not limit deep breathing or coughing; the incisional pain after thoracotomy or cholecystectomy interferes with deep breathing and coughing.

The surgical procedure and postoperative pain are undeniable facts. It is in the postoperative period that the patient's capacity to protect his ego is deranged. His ability to perceive the situation may be blunted by emergence from anesthesia, by pain, by narcotics given to relieve pain, and by confusion as to what has happened. The inability to respond to the satisfaction of his attendants may frustrate and infuriate him and lead him to the conclusion that it is just too much trouble to apply himself to the task at hand. He may be further frustrated or depressed by hearing what is said yet being unable or disinterested in making himself clearly understood. The symbolic significance of the operation, especially a mutilating one, may be a devastating blow to his ego defenses. At this time the patient needs all the support he can get.

It is difficult to predict accurately the patient's psychological response to operation and postoperative pain because pain is a psychologic experience based on memories and patterns of behavior as well as on sensory perception. Fortunately during the preoperative preparation the patient usually reveals many cues either consciously or unconsciously, verbally or nonverbally, as to how he will react postoperatively. In collecting and assessing these cues before operation the physician must be prepared to listen sympathetically to fears, wishes, fantasies, memories, anxieties, and dreads of the impending surgical procedure.

The chances are overwhelming that the patient will use the complaint of pain in the postoperative period exactly as he used his pain or other symptoms before operation. How has the patient learned to complain or not to complain? How has the patient used his symptoms before operation either for secondary gain or to relate to others? Since the anesthesiologist is evaluating the patient in relation to the impending anesthesia, he is not primarily concerned with the patient's symptoms nor what his complaints have been preoperatively. Therefore, he may not get an accurate picture of how the patient complained or used his symptoms. He often has to rely on secondary clues from nursing personnel, relatives, and roommates. Hunches in this regard are risky. Hence, a few appropriate words on the patient's chart by the referring internist or surgeon can be very helpful.

Emotionally labile or volatile patients fear pain and become distraught by the pain when it is felt. But when their pain is relieved, they forget their suffering. Other patients who are intelligent and contemplative express their anxiety about the significance of the pain. These are the ones who are prone to morbid ruminations about the cause, meaning, and outcome of pain as well as the measures taken to combat it. After pain has been relieved in such persons, they are likely to be depressed because of the fear that the pain has been controlled but the disease uncured. One can manage these patients by telling them in advance where they will feel pain postoperatively, its probable duration, and at the same time reassure them that pain relief will be available when needed. Accurate and tactful prediction goes a long way to establish confidence in the physician.

The patient emerging from anesthesia unprepared for the pain he is experiencing or the mutilation he has undergone may react by becoming depressed, confused, or recalcitrant. Such a patient should not

be expected to cooperate or exert himself. Therefore, if he is to participate effectively postoperatively, his physicians must avoid setting the stage for confusion or depression. They must tailor their program to the patient and educate him to participate effectively. For example, he may be told that the Recovery Room nurses will ask him to breathe deeply and to cough. Although the nurses will sound as if they are in the next room or down the hall, they are talking to him. One might further emphasize that by taking deep breaths and coughing he will awaken more quickly.

Anxiety

The third element is to assess what ego defenses the patient uses and how he uses them preoperatively, and their implications for the postoperative period. Abram and Gill found that the patient's preoperative level of anxiety, his expectation of surgery, and his use of denial correlated well with his psychologic postoperative course. Patients who had a moderate degree of preoperative anticipatory fear did well psychologically postoperatively. On the other hand, those with a little or those with much anticipatory fear were more likely to develop emotional troubles postoperatively. Such patients usually become confused, depressed, and uncooperative, and thereby thwart the best therapeutic efforts of their physicians. Hence, it is crucial to assess the preoperative level of anxiety.

In searching for anxiety, one must determine if the patient has come to terms with his situation maturely or if a bravado masks terror. A short discussion often suffices to make the distinction. The astute physician recognizes undeclared anxiety on shaking the patient's cold, clammy hand and in observing his facial expressions and vasomotor changes and fidgeting of his fingers and hands. The content and tenor of the patient's questions about anesthesia and emergence pinpoint the areas of his anxiety and paint a graphic picture of his anxiety.

The tense, frightened, anxious patient represents a true challenge because his desire for psychologic calm is thwarted by inappropriate defenses. In this situation, hypnosis may permit the anesthesiologist to establish rapport rapidly. It allows the patient to ventilate under the aegis of the trance with or without amnesia. Furthermore, the anesthesiologist is able to make suggestions for relaxation and calm fears, as well as give posthypnotic suggestions about deep breathing and coughing postoperatively without "discomfort." The semantic device of substituting "discomfort" for "pain" circumvents the patient's store of memories of pain and hopefully deprives him of his stereotyped reactions to the word.

Even if the patient does not attain the trance state, use of the hypnotic technique lets the anesthesiologist capture and focus the patient's attention on the anesthesiologist's suggestions. This diverts the patient's attention from consuming anxiety and often this respite from anxiety establishes rapport for the anesthesiologist.

Realistic Expectation

The surgeon must present the operation to the patient realistically. Janis found those patients who had a realistic expectation of the operation did well postoperatively. Those who did not have a realistic expectation of surgery, either because of the surgeon's failure to communicate before operation or because they used denial to effectively block communication, were surprised, disappointed, and aggrieved after the operation. Such patients are likely to become confused, depressed, and uncooperative. This lack of cooperation postoperatively can thwart the best therapeutic intentions. Since denial is known to be an effective barrier to realistic communication, the physician must differentiate clinically between a brave exterior and denial.

Egbert and associates have extended the concept of realistic appraisal to the impending anesthetic experience and have successfully demonstrated that premedication alone cannot allay preoperative apprehension. Patients who had received a preoperative barbiturate but who did not have a preanesthetic visit were drowsy but not necessarily calm. Patients who had been informed by an anesthesiologist on his preanesthetic rounds of the sequence of events to occur on the operative day but who had *not* received a barbiturate as preoperative sedation were calm even though not drowsy. To explain how a short preanesthetic interview the night before operation could exert such a profound effect, they drew on the extensive work of Janis. Those who face an anxiety generating situation look for emotional support. "An authority, supposedly able to modify the danger, becomes invested with strong emotional significance. The statements made by this authority assume greater importance than would ordinarily be expected." Although only a brief interval is traditionally accorded to the anesthesiologist, yet by virtue of the patient's psychologic situation the anesthesiologist has a unique set of circumstances in his favor. He has the potential to help the patient a great deal in a relatively few

minutes. He may be able to initiate on his preanesthetic visit a preoperative program for the prophylaxis of postoperative pain.

Denial

Denial of fear, anxiety, and the results and implications of the impending operation and anesthesia is a common ego defense potentially pernicious both physically and psychologically. It is likely to appear in those who have placed a premium on an adult and independent role in life, who fear the threat of invalidism, and who have shown an unusual capacity to deny or minimize unpleasant reality throughout their lives. When the patient totally denies the clear implications of the impending operation, then denial tends to the psychotic. The anesthesiologist may recognize the danger signals of denial in the average patient, but in the more sophisticated he may miss them altogether. Since the internist and the surgeon have known the patient for a longer time and participated in a variety of experiences with him, they are in the best position to diagnose the pathologic use of denial and request a preoperative psychiatric consultation. A refusal to be concerned by remote possibilities or to minimize unimportant details or restrictions of the therapeutic regimen is not denial.

The excess use of denial as an ego defense carries with it a clear implication that the patient has a low tolerance to stress. We can predict before operation that postoperative pain will unduly distress such a patient. These are the patients who will not breathe deeply and will not cough after operation and who demand or wheedle narcotics for pain. They refuse to cooperate with a stir-up regimen; consequently they invite atelectasis, pneumonia, lung abscess, urinary retention, and ileus.

Knorr points out that denial has one *useful* facet which is often overlooked. Patients who undergo mutilating operations such as those resulting in a colostomy, loss of a breast, hysterectomy, amputation, or facial deformity, are more likely to suffer a depression or other psychologic problems postoperatively. In this group, we can predict with some assurance a psychologically stormy postoperative course. When this is coupled with the pain following extensive surgical procedures, a potentially difficult problem in postoperative management can be predicted. Denial can be an important mechanism in reducing the degree of depression in these patients. Therefore, confronted with the need for mutilating operations, it behooves the physician not to circumvent the patient's denial, but to manipulate it for the patient's benefit.

Other Studies

So far the preoperative, psychologic evaluation of the patient has been stressed from the point of view that this is the foundation upon which a preoperative prophylaxis of postoperative pain can be built. By contrast, it may be interesting to examine a program which was confined entirely to the postoperative period. This study confirmed only two cases of postoperative atelectasis in 2,478 patients. Deep breathing and coughing were the mainstay of the program. "If (the patient) is unable to breathe deeply unassisted, the anesthesiologist must aid him by means of painful stimuli or positive pressure by mask." Any of five pressure-pain sites were stimulated and all personnel were imbued with the need for repetitive stimulation of these sites to make the patient breathe deeply. Several techniques to stimulate coughing in the obtunded or recalcitrant patient were outlined. The impression is gained that more rather than less pain was needed to make the postoperative patient breathe deeply and cough. The preoperative period was ignored.

Some studies have attempted to reduce the amount of narcotics needed to manage postoperative pain by a sympathetic and extensive *preoperative* preparation of the patient. Roe was able to reduce the total postoperative narcotic dosage from 50 to 100 mg. of morphine or its equivalent to 4 mg. or less. Egbert and associates were able to significantly decrease the amount of narcotic needed on postoperative days one to five but not on the day of operation. In both series the patients were told preoperatively that pain was to be expected postoperatively and was not abnormal. Furthermore, the patients were assured pain medication would be available when requested. Roe emphasized to his patients that their wounds would be securely closed and their deep breathing and coughing would not disrupt the incision. Techniques of deep breathing and coughing were taught, and, when required, patients were familiarized with the use of a positive-pressure apparatus preoperatively. After operation, the physicians visited, assisted, and encouraged their patients to use the techniques taught. In short, the physicians educated their patients preoperatively and encouraged them postoperatively to participate in the therapeutic program.

Although not explicitly stated, the physicians in these studies were as attentive to their patients'

welfare before as after operations. The patient-physician relationship evolved during the preoperative period was extended to and used to support the patients postoperatively.

Summary

To avoid the complications of postoperative pain and the drugs used to treat it, the physicians who care for the preoperative patient must develop a supportive relationship with him looking to the postoperative period. They must not only support the patient but they must also teach him how to participate effectively in the period after operation.

To support the patient, they must determine the effect of the impact of anesthesia, surgery, and postoperative pain as well as the meaning of the operation on the patient's psyche. Guidelines to such an evaluation are the patient's responses and reactions to pain in the past, the level of the patient's anxiety, his use of denial as an ego defense, and his expectations of surgery. Having this information at their disposal, the physicians can then tailor a preoperative program for the prophylaxis of postoperative pain to the needs of the patient.

(The references may be seen in the original article.)

CERAMIC GLAZE AS A SOURCE OF LEAD POISONING

Robert W. Harris, MD, and William R. Elsea, MD, JAMA 202(6):544–546, Nov 6, 1967.

Plumbism occurred in a patient after he had used a lead-glazed drinking vessel. Apparently, sufficient lead was leached from the mug's glazed inner surface by a soft drink with a pH of 2.7 to result in clinical saturnism after two years of habitual exposure. Laboratory and experimental studies confirmed the available quantity of lead in the source. Similar cases of lead poisoning resulting from the use of acidic food or drink with lead-glazed utensils have occurred in the past.

Although some recent reports have attributed the catastrophic downfall of the Roman empire to infertility, stillbirths, high neonatal mortality, and attrition of the aristocracy by several generations' exposure to toxic amounts of environmental lead, in more recent years only isolated cases and smaller-scale epidemics of plumbism have been recorded. It is now generally agreed that most pediatric cases of lead poisoning are the result of pica for leaded paints, especially among lower socioeconomic groups; but most adult cases, other than those of industrial etiology, result from widely varying, often obscure, lead sources. Although not strictly representing a new entity or cause of saturnism, we believe this case is unique in some facets, and may portend a larger-scale potential danger.

From the Epidemic Intelligence Service, Epidemiology Program, National Communicable Disease Center, Public Health Service, Atlanta (Dr. Harris), and the Erie County Health Department, Buffalo (Dr. Elsea).

Read before the annual Epidemic Intelligence Service Conference, Atlanta, April 13, 1967.

Reprint requests to 601 City Hall, Buffalo 14202 (Dr. Elsea).

Report of a Case

After a relatively uneventful recovery from a well-documented myocardial infarction, the patient, a 55-year-old physician, was hospitalized with hepatomegaly and progressive erythropenia. The patient noted a history of generalized fatigue, sensations of heaviness in both arms, insomnia, headaches, anorexia, nausea without emesis, occasional loose stools, and a 10-lb weight loss, over a one-month period. He also complained of intermittent crampy abdominal pain of several weeks' duration, but denied any history of ethanolism, or known exposure to hepatotoxins or to icteric patients. Physical examination on admission to the hospital revealed a blood pressure of 170/100 mm Hg; pulse rate, 68 beats per minute; a grade II hypertensive retinopathy; and a smooth, firm, nontender liver edge palpable 4 cm below the right costal margin. There were no other significant abnormal physical findings. Significant laboratory results included the following: hemoglobin level, 11.5 gm/100 ml; hematocrit reading, 34 percent; white blood cell count, 6,800/cu mm; serum glutamic oxaloacetic transaminase (SGOT) activity, 204 units; serum glutamic pyruvic transaminase (SGPT) activity, 245 units; total bilirubin level, 1.2 mg/100 ml; alkaline phosphatase level, 11.1 units/100 cc; and albumin-globulin ratio, 3.8:2.4. The fasting blood glucose level was 117 mg/100 ml, and the blood urea nitrogen level was 14 mg/100 ml. Results of urinalysis were normal. In comparison, the follow-

ing values were obtained one month prior to admission: hemoglobin level, 15.2 gm/100 ml; hematocrit reading, 42 percent; and SGOT activity, 18 units. After the patient had been hospitalized for one week, the hematocrit reading had fallen from a previous high of 42 percent to 30 percent; it was at this time that the initial discovery of hypochromic erythrocytes with polychromatophilia and abundant basophilic stippling was made. A bone-marrow specimen taken at this time also revealed marked basophilic stippling as well as numerous target cells, with somewhat increased numbers of red cell precursors. The level of coproporphyrin in the urine was 804μg/24 hr (the normal upper limit is about 100μg/24 hr). Two 24-hour urine collections demonstrated lead concentrations of 330 μg/liter and 720μg/liter (150μg probably indicating a dangerously high level of absorption). Even after two-weeks' hospitalization, and presumed total abstinence from exposure to the toxic source, the level of lead in the blood was 58μg/100 gm (80μg/100 gm of whole blood represents a potentially dangerous level). It was felt that the history and laboratory data established a probable diagnosis of lead poisoning.

The patient began a five-day course of therapy with edetate calcium disodium (Calcium Disodium Versenate), during which he excreted over 2 mg of lead in the urine. Ten days after therapy, the level of lead in the urine had fallen to 18μg/liter. Three months after therapy was initiated, the hematocrit reading had risen to 42 percent, but a random sample of urine contained 80μg of lead per liter, and the lead level in the blood was 73μg/100 gm. Hence, a second course of therapy was initiated. Three months later, the concentrations of lead in the urine and blood were well within normal limits. Similarly, by this time, the SGOT, total bilirubin, and alkaline phosphatase levels had all returned to normal.

Comment

It is less well known but previously demonstrated that increased lead ingestion (even without overt poisoning) may result in transaminase levels as high as 400 units, presumably secondary to hepatic dysfunction. Previous cases of plumbism with hepatomegaly or hepatic dysfunction or both have been noted in the literature. Considering the significant role of hepatic storage of lead during pathological absorption and its probable toxic effects on the liver, this is not surprising. Elevated serum bilirubin levels have also been noted previously, perhaps attributable to hepatic involvement or a hemolytic process or both. Unfortunately, a simultaneous reticulocyte count was not obtained in our case. The elevated alkaline phosphatase level may similarly reflect the hepatotoxic effect of lead. Questioning for possible sources of lead at first seemed futile, but the patient's wife soon offered the key clue to the mystery. It seems that the patient had the unique habit of filling a ceramic mug, made by his son, with ice and a soft drink. He sipped the chilled soda during a period of several hours in the evening, usually refilling the mug with a second bottle of cola. This had been an almost nightly ritual for the two years preceding his admission to the hospital.

Examination of the mug soon revealed ample cause for suspicion. The patient's drinking mug was forwarded to the Kettering Laboratory, University of Cincinnati School of Medicine, for toxicological examination. It was demonstrated that over 5 mg of lead was leached from the mug per 450 cc of cola after only 30 minutes. A mug identical to the one used by the patient was forwarded to us by his son. This yellow ceramic mug or "glass" stands 16 cm tall, has a maximum diameter of 9 cm, and holds 600 cc of liquid. The outer surface has a lustrous, smooth-glazed finish, but the inside is quite faded and has a chalky, almost crystallized surface. When the vessel was filled with chilled cola, which has a pH of 2.7, there was a very rapid appearance of lead in the soft drink. Within just two minutes after adding the cola, there was 0.3 mg/100 cc or about 1.5 mg of lead leached from the mug per bottle. After two hours in the glass, the lead level was as high as 0.68 mg/100 cc. No lead was noted when the mug was filled with water, and, of course, a control test of the cola demonstrated only 0.02 mg of lead per 100 cc. When the exterior of the mug was bathed in the chilled soft drink, within 15 minutes, the lead concentration was nearly 0.2 mg/100 cc. Even after this brief exposure, there was slight but definite decolorization of that part of the mug immersed in the cola.

As seen in the Figure, the two series of lead determinations differed considerably from each other, yet the averages of the five values in each series were 0.39 and 0.36 mg lead per 100 cc of cola. With the latter value as an example, the patient would have consumed approximately 1.6 mg of lead per bottle of cola, or up to 3.2 mg per night (remembering the patient's habit of consuming two 450-cc bottles of cola each evening). This would give a total intake of more than 2 gm of lead over the two-year period of presumed exposure. Kehoe

has demonstrated with tests on volunteers that within eight months a daily ingestion of 3 mg lead, in addition to "normal" dietary lead, would result in dangerously high concentrations of lead in the urine and blood.

Hence, the amount of lead necessary to produce potentially toxic levels in Kehoe's experimental study correlates rather closely with our estimate of the amount of lead consumed by the patient in this case report. Beritic and Stahuljak pointed out that as much as 20 to 30 gm of lead may be used to glaze even a small pot. Thus, the probable ingestion of 2 gm of lead or more by this patient—although having severe pathologic results—represents probably only a small percentage of the lead contained in the mug's glaze.

The patient's son had molded several identical mugs while enrolled in a ceramics class at a Buffalo college. They apparently were intended to be used as vases, but were found to be quite handy as drinking mugs. His was one of the few classes to use lead oxide as the glazing agent on ceramic projects. This glaze was prepared by the students, following a "cookbook recipe," although it was applied and fired by the instructor. The students were forewarned of the dangers in handling lead glazes, but relatively little, if anything, was mentioned about the actual use of the resulting articles. We are now in the process of contacting all other members of this class, even though the school has banned the general use of lead-base glazes in the future. This very high concentration of lead, and the reported ease with which the glaze was compounded by the students probably indicate the use of a nonfritted, more soluble, leaded glaze. Commercially produced dishware is usually glazed with a fritted and much less soluble type of lead glaze which yields only 2 percent to 5 percent soluble lead, as opposed to the 20 percent to 30 percent lead occasionally seen in improperly glazed items.

In reviewing the literature, it became clear that numerous similar experiences with acidic food or drink and lead-glazed utensils have been noted in the past—and actually as far back as the time of the Roman empire, when lead was abundantly used not only in cooking utensils, but also to adulterate wine. More recently, in California in 1958, imported ceramic dishware was noted to be decolorized when exposed to acid fruits. In this instance, improper firing was thought to have resulted in a loosely adherent glaze, which was then readily dissolved and decolorized by the acidic medium. In March 1967, chronic gastrointestinal illness in Mexico was ascribed to poorly fired, lead-glazed earthenware (*Medical World News* 8:21 [March 3] 1967).

Even though our isolated case of lead poisoning might at first be regarded as a relatively insignificant indication of danger to the public health, the popularity of ceramics as an art and a hobby, and the paucity of governmental regulation would seem certainly to offer a potentially dangerous situation, considering that the ceramics industry uses some 25,000 to 30,000 tons of lead per year.

Robert A. Kehoe, MD, performed toxicological studies.

Generic and Trade Names of Drug

Calcium disodium edetate—*Calcium Disodium Versenate.*

(The omitted figure and references may be seen in the original article.)

ABDOMINAL AORTIC ANEURYSMS

CLINICAL STATUS AND RESULTS OF SURGERY IN 100 CONSECUTIVE CASES

Sandor A. Friedman, MD, Charles A. Hufnagel, MD, Peter W. Conrad, MD, Earl M. Simmons, MD, and Alan Weintraub, MD, JAMA 200(13):95–102, June 26, 1967.

Of 100 patients who underwent elective resection of abdominal aortic aneurysms, most had been asymptomatic, but about one third had had symptoms referable to the aneurysms. In 19 percent of the cases, the aneurysms were found on roentgenograms taken for other reasons. There was high prevalence of other cardiovascular abnormalities. Peripheral arterial occlusion and myocar-

dial infarction were the most serious complications in the survivors and occurred only in patients who had prior evidence of arterial occlusion. In particular, patients with angina and peripheral arterial occlusion had the greatest incidence of complications. The surgical mortality was 4 percent. The bleak outlook for patients with aneurysm which is not corrected by operation makes it necessary that this diagnosis not be overlooked in the general examination of patients.

Although aneurysmal dilatation of the abdominal aorta is a well-recognized entity, little is known of the factors promoting this degeneration except that it is clearly associated with other manifestations of the atherosclerotic process. Since MacVaugh and Roberts pointed out the dire prognosis of untreated aneurysms and the marked improvement in life expectancy after successful resection, surgical techniques in handling the aorta have improved. However, when other problems such as coronary artery disease are present in an individual with an aneurysm, it may be difficult for physicians unfamiliar with this problem to decide whether the risks outweigh the possible gains of surgery.

In order to study the clinical features and factors involved in the surgical risk for aneurysm patients, we have reviewed the clinical records of a consecutive series of patients operated on electively for unruptured aneurysms at the Georgetown University Hospital.

Material

One hundred consecutive patients who underwent elective resection of abdominal aortic aneurysms during the period from June 1965 to February 1966 are included in this study. Prior to surgery all patients were carefully evaluated, special consideration being given to the cardiovascular system. Any possible complicating factors were followed up by thorough evaluation of the involved system.

Resection of the abdominal aneurysm was performed with replacement of the aorta and common iliac arteries with uncrimped "Halanca"-woven Dacron prosthesis. Endarterectomy or thromboendarterectomy was performed when indicated in the individual case. All patients received an infusion of 10 percent mannitol prior to and during aortic clamping.

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The distal anastomosis was carried out after the proximal anastomosis was secure, and circulation was established in one leg prior to completing the anastomosis in the remaining leg. Bilateral lumbar sympathectomy was also usually performed. The vital signs and electrocardiogram were monitored during the procedure and postoperatively until the patient's cardiovascular status was stable. All patients were carefully evaluated preoperatively and followed up postoperatively by a member of the cardiology service as well as the surgical team, and postoperative ECGs were routinely done.

Clinical Manifestations

These patients were generally of the older age groups, with an average age of 67 years; only two were under age 50. Eighty-three percent were men.

Although most of the patients had been asymptomatic in regard to their aneurysms, careful questioning revealed symptoms that could be related to the aneurysm in 34 percent (Table 1). (Symptoms that seemed related to gastrointestinal or urological problems have been discounted.) Generally, the abdominal pain was described as relatively dull, steady and unrelated to activity or eating, although one patient gave a convincing history for abdominal angina, two patients described crampy pain, and two related pain to movement. Back pain was generally felt as radiation from the abdominal area except in three, who had only back pain. The fact that 11 patients were aware of a pulsation or pounding in their abdomen suggests that this is a useful question to ask when the presence of an aneurysm is suspected. On the other hand, 59 percent had no abdominal symptoms at all, their aneurysms having been found during routine examinations or while being followed up for some other problem.

The aneurysm was readily palpable in all but 10 percent and visible on plain films (anteroposterior or lateral) of the abdomen in 60 of 83 cases (72 percent). Another seven roentgenograms were read as possibly showing an aneurysm. Four patients, all of whom were referred because of peripheral arterial disease, had neither a palpable aneurysm nor roentgenographic evidence of it (three having aortography performed), but the aneurysm was found at the time of surgery. Two of these patients were obese, however, limiting the accuracy of abdominal examination, and all four had small aneurysms. The value of plain films is further demonstrated by the fact that 19 aneurysms were discovered as incidental findings on plain films taken for

TABLE 1.—*Clinical Manifestations of Aneurysm*

Sex	No.	Average Age, Yr	Total With Symptoms	No. With Abdominal Pain	No. With Back Pain	No. With Pulsation In Abdomen	No. With Feeling of a Mass
M	83	67 (46-84)	29	16	12	10	5
F	17	67 (53-83)	5	5	2	1	1

other reasons and on scout films of five upper gastrointestinal series, one barium enema, one oral cholecystogram, and one intravenous pyelogram. In 99 patients the entire aneurysm was found to be distal to the renal arteries at the time of surgery.

Associated Cardiovascular Findings

The overwhelming number of patients (88) in this series had associated cardiovascular disease. The presence of clinically evident coronary artery disease in 47 percent (Table 2), as compared to an expected figure of about 10 percent (Table 3), emphasizes the widespread vascular involvement. Nineteen of these patients gave a history of previous myocardial infarctions, and 15 had been having intermittent bouts of angina pectoris at the time of admission. Thirty-two of the 47 had electrocardiographic evidence of coronary artery disease. The criteria for establishing the electrocardiographic diagnosis of coronary artery disease were the following: significant Q waves indicative of old infarcts (16); left bundle branch block (2); left axis deviation past 120° in the absence of hypertension or valvular heart disease (5); and symmetrical T-wave inversions and ischemic S–T depressions not caused by digitalis or electrolyte imbalance (13). In addition to the above, ten patients with a normal history and a normal ECG had, on cardiac auscultation, a definite quadruple rhythm with atrial and ventricular diastolic gallops without systemic hypertension or aortic stenosis, suggesting myocardial disease. These figures possibly underestimate the frequency of angina pectoris, since the amount of exercise performed by many of these patients was severely limited by other symptoms such as intermittent claudication and dyspnea.

TABLE 2.—*Frequency of Other Cardiovascular Disease* *

	Coronary Artery Disease	Peripheral Arterial Obstruction	Cerebrovascular Disease	Hypertension
Coronary artery disease	47	18	4	19
Peripheral artery obstruction	18	43	6	15
Cerebrovascular disease	4	6	8	5
Hypertension	19	15	5	34
Total with cardiovascular disease 88				

* The number in each box represents the frequency of coexistence of the disease listed above it and the disease listed to the left of it.

TABLE 3.—*Estimated Prevalence of Some Cardiovascular Diseases in the United States* *

Disease	Age Range, Yr 45-54	55-64	65-74	75-79
Coronary disease	M 4% F 2%	M 10% F 5%	M 11% F 8%	M 9% F 5%
Hypertension (as defined in this paper)	M 11% F 11%	M 13% F 21%	M 16% F 25%	M 35% F 16%
Cerebrovascular disease †	M 0.8% F 0.7%		M 4% F 3%	

* Data from the National Center for Health Statistics (also from an interview survey, unpublished, from the same agency).

† Prevalence figures for cerebrovascular disease represent 20- rather than 10-year intervals.

The finding of some definite evidence of peripheral arterial obstruction in 43 percent of the patients is consistent with a widespread disease process. One special consideration is the fact that in 27 of these 43 subjects, the obstruction appeared to be distal (in the femoropopliteal area). The majority of these patients had no symptoms of arterial insufficiency, 18 having claudication and one complaining of ischemic pain at rest. Again, the paucity of symptoms in the lower extremities is related to limited physical activity produced by cardiac or pulmonary disease or by both. Patients were classified as showing significant peripheral arterial obstruction if one of the following criteria was met: (1) absence of one or more of the major pulses (femoral, popliteal, or posterior tibial), (2) pulses definitely weaker in one extremity than the other, or (3) weakness of femoral and/or popliteal pulse bilaterally with claudication.

The absence of a dorsalis pedis pulse was not considered diagnostic unless it was a unilateral loss,

and a generalized weakness of pulses without symptoms was not accepted as evidence of arterial obstruction. An additional three patients had femoral artery bruits without significant obstruction. Although the true prevalence of peripheral arterial obstruction in the general population is not known, Mahmoud estimated rates of 6 percent and 3 percent, respectively, for intermittent claudication in men and women in the age range of 55 to 74 years.

The eight patients with cerebrovascular disease had suffered cerebrovascular accidents or had symptoms such as a sudden hemiparesis, expressive aphasia, diplopia, and vertigo, which can be referred to as transient ischemic attacks. In addition, there were six patients with carotid bruits.

In this retrospective study, hypertension was defined as a blood pressure in the arm greater than 160/90 mm Hg on several determinations, diastolic pressures of 100 mm Hg or more, or documented elevations of blood pressure at this level in the past if the patient was normotensive and taking antihypertensive medication at the time of admission. The prevalence in 34 percent of our patients is almost twice the expected figure, as shown in Table 3. Although the frequency of hypertension might be explained by the known relationship between hypertension and atherosclerosis obliterans, hypertension was also found to be present in 7 (28 percent) of the 25 patients without evident coronary, cerebral, or peripheral arterial occlusion. It thus appears that abdominal aortic aneurysms may be specifically related to hypertension, although no attempt at correlation can be made in this study.

Thoracic Aorta.—Chest films demonstrated abnormalities of the aortic shadow in 81 percent of these patients. Calcification was seen in 26 percent and dilatation in 19 percent of the thoracic aortas. The remaining abnormalities consisted of tortuosity and elongation. Although the latter findings are not unusual for an elderly population with a high prevalence of arterial occlusive disease, the frequency of dilatation seems to be high and suggest that weakening of the aortic wall with subsequent dilatation is a generalized process. However, it has been our experience that dilatation of the thoracic aorta generally does not progress to aneurysm formation.

Pulmonary Disease.—As one might anticipate in a relatively elderly group of patients, obstructive emphysema was a common finding. A total of 36 percent had findings either on physical examination or on chest x-ray films or on both of emphysema, although only 11 complained of dyspnea. This figure corresponds closely to Schlesinger's finding of hypertrophic emphysema in 25 percent to 50 percent of autopsies of elderly patients.

Diabetes Mellitus.—Fasting blood sugar levels were determined for 83 patients, 15 of whom also had sugar levels measured two hours postprandially. Although only six patients gave a history of diabetes, abnormalities were found in 22 (27 percent). Three other patients receiving therapy had normal blood sugar levels. This finding, of course, does not represent the true frequency of diabetes, since testing for abnormal fasting sugar concentrations was not repeated in most cases and since most of the patients with normal fasting levels did not have two-hour postprandial determinations. However, even this crude figure indicates that diabetes is very prevalent in these patients. (The estimated prevalence of diabetes in the United States in this age group is between 3 percent and 6 percent.) It is difficult to know whether occurrence of diabetes is related to the occlusive arterial disease only or whether there is also some relationship specifically to aneurysms. Of the small group of 19 patients studied without occlusive disease, four (22 percent) had abnormalities. Although this is a high prevalence figure, the number of patients involved is too small to allow any definitive statement.

Platelet Count.—In 29 patients who had platelet concentrations determined by direct counting, the range was from 108,000 to 565,000/cu mm, normal for the laboratory being 150,000 to 300,000/cu mm. Nine were above and two below normal. When an attempt was made to compare the frequency of occlusive disease with the level of the platelet count, no correlation could be made. Although the number of counts done is small, this high percentage out of the normal range should warrant further investigation.

Surgical Mortality and Morbidity.—Four patients (all men) in this series died following surgery. One died ten days postoperatively in shock, congestive heart failure, and renal failure after showing electrocardiographic changes of an acute myocardial infarction. Although he had no history of coronary disease, and his ECG was normal, he did have severe peripheral arterial disease with ½ block claudication distance.

A second patient suffered a cerebrovascular accident with hemiparesis and coma and died on the 22nd postoperative day. This man also had claudication and, in addition, a left bundle branch block, but no history of angina, previous infarct, or neurological difficulty.

In a third patient, a sudden popliteal artery occlusion with severe ischemia developed on the first postoperative day and had to be explored again for removal of clot. Following the second operation, shock and oliguria developed, and the patient died on the second postoperative day. He had diffuse arterial disease, having had claudication for two years and a history of transient hemiparesis two months before admission. His ECG showed marked left axis deviation and stable T-wave inversions in the left precordial leads.

The fourth patient died 12 hours postoperatively after suffering cardiac arrest three times. He had shown no previous evidence of obstructive arterial disease in the coronary, peripheral, or cerebral circulations.

In Table 4, fifteen cardiovascular complications are shown for the 96 surviving patients. Occlusion of the arteries of the lower extremities, the most frequent complications, occurred in five patients. In four the occlusion was confined to the femoropopliteal area and probably resulted from embolization of clot in the aneurysm or parts of atherosclerotic plaques in the vicinity. Iliac obstruction developed in the fifth patient. In three of these cases, dissection of the aneurysm away from the inferior vena cava had been very difficult. In two patients severe ischemia developed postoperatively, requiring embolectomy, one ultimately having an amputation; the other three patients required only conservative management. Two of the five had peripheral arterial disease preoperatively, and four had coronary disease.

Four patients had myocardial infarctions within the first week after operation, clearly demonstrated by ECG and serum enzyme changes. Three had no chest pain, and all recovered uneventfully. All appeared to have widespread arterial occlusion and active heart disease. Three had evident coronary disease preoperatively, with a history of angina and ischemic S–T and T changes on their ECGs, one of them also having a history of a myocardial infarction and the other two, peripheral arterial disease. The fourth had a long history of hypertension and had required digitalization for congestive heart failure several years before this admission. In another patient with coronary and peripheral arterial disease, cardiac arrest developed during surgery. He had a two-month history of angina and an ECG showing left axis deviation. Although resuscitation was successful, resection of the aneurysm was not carried out. In addition, eight patients had transient electrocardiographic evidence of ischemia during the first few postoperative days. Five of this group had coronary disease, and one, peripheral arterial disease, only two being free of overt arterial obstruction.

TABLE 4.—*Complications of Surgery in 96 Surviving Patients*

Complications	No.
Peripheral arterial occlusion	5
Myocardial infarction	4
Supraventricular arrhythmias	3
Cerebrovascular accident	1
Cardiac arrest	1
Pulmonary embolus	1
Pneumonia	1
Massive atelectasis	1
Partial wound dehiscence	3
Wound infection	1
Upper gastrointestinal tract bleeding	1
Acute renal insufficiency	1
Foot drop	1

Supraventricular arrhythmias developing in three patients were easily treated with digitalis and quinidine. All had prior evidence of coronary and peripheral arterial disease. The one patient who had a cerebrovascular accident made a good functional recovery. He had a history of transient ischemic attacks.

Comment

It has generally been accepted that patients with abdominal aortic aneurysms are often asymptomatic until the point of rupture. This series substantiates the evidence for the asymptomatic nature of most unruptured aneurysms, but also demonstrates that significant clues to the diagnosis can be obtained from a minority by careful questioning. Of particular importance are the complaints of vague pain and a sense of pulsation in the abdomen. Such symptoms in a middle-aged individual, even in the absence of a palpable aneurysm, would appear to be an indication for obtaining anteroposterior and lateral abdominal films. In fact, these roentgenograms might have utility in adult health screening clinics, since an aneurysm apparent by roentgenogram may be missed on physical examination, as illustrated by the 19 patients in this series whose aneurysms had been diagnosed first by an x-ray film.

The finding of at least some minor evidence of other cardiovascular disease in all but a few patients clearly implies that there are factors common to both obstruction of arterial lumens and weaken-

ing of their walls. Hypertension appears to be one, and diabetes may be another.

There appear to be, however, some important distinguishing features. First, the average age of 67 years in this series is much greater than that (49 years) reported for patients first presenting with aorto-iliac obstruction. Secondly, of the 43 patients with peripheral arterial disease, only 16 percent (7) appeared to have predominantly aorto-iliac obstruction. These findings suggest that there may be some etiologic differences between the two types of arterial disease. Furthermore, one of the serious complications of this operation appears to be embolization to the femoral and popliteal arteries. This fact, together with the low prevalence of aorto-iliac obstruction, points to the possibility that embolization to these arteries from clot or calcium, that is almost invariably present in the aneurysms, contributes to the high frequency of femoral and popliteal occlusions found in these patients.

Although mortality figures vary, the poor prognosis of patients with untreated aneurysms is clearly established. Previous reports have demonstrated a steady improvement in the surgical outlook. The operative mortality of 4 percent and low incidence of serious morbidity in this series indicate that resection of unruptured abdominal aortic aneurysms located below the renal arteries can now be performed relatively safely despite the presence of significant occlusive arterial disease in the vast majority of these patients. Although patients with aneurysms above the renal arteries are still subject to a high surgical mortality, the rarity of this type of involvement is illustrated by the finding at surgery that only one of 100 aneurysms in our group extended proximally to the level of the renal vessels.

The surgical mortality appeared to be unrelated to the presence of coronary heart disease. In fact, none of the four patients who died had symptomatic heart disease, although three had peripheral arterial disease and two had abnormal ECGs. This occurrence may have been fortuitous, since the total number of deaths and number of patients without evident arterial occlusion were both small.

On the other hand, postoperative morbidity was highly correlated with the presence of prior coronary, peripheral, and cerebral arterial obstruction. With the exception of the transient appearance of ischemic ST–T changes in the ECGs of two patients, there were no cardiovascular complications in the 24 surviving patients initially not found to have definite occlusive disease. Of the five patients with serious cardiac complications, four had angina pectoris preoperatively. The patient in whom cardiac arrest developed had had angina for only two months, and it is conceivable that his coronary disease was in an unstable situation at the time of surgery. It appears that the presence of angina is a very significant factor in morbidity, since six of 15 with this symptom had some postoperative difficulty. The diagnostic significance of routine postoperative ECGs is well demonstrated by the findings of three asymptomatic myocardial infarctions and eight cases of transient ischemic changes.

The other frequent complication, arterial occlusion of the lower extremities, appeared only in patients with coronary or peripheral arterial disease or with both. One other patient who had a temporary foot drop without loss of pulses also had coronary disease. Although surgical trauma may have been an important factor here, it is possible that embolization was made easier by stagnant flow produced through partially obstructed vessels and reduced cardiac output. The use of agents such as low molecular-weight dextran to improve peripheral flow may diminish the frequency of this complication in the future.

With the improved surgical outlook for patients with abdominal aortic aneurysms, it now becomes imperative not to miss this disease in the examination of middle-aged and elderly patients. Moreover, careful abdominal palpation for aneurysms, combined with anteroposterior and lateral films of the abdomen in obese patients or in those with difficult abdomens to examine, might be a valuable addition to many screening clinics such as those for diabetes and hypertension. Certainly, it is one of the most important items in the examination of the cardiovascular system.

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Generic and Trade Names of Drug

Dextran—*Expandex, Plavolex.*

(The references may be seen in the original article.)

FOUR YEARS EXPERIENCE WITH IMPLANTED CARDIAC PACEMAKERS*

Richard A. Carleton, MD,[1] Robert W. Sessions,[2] Milton Weinberg, MD,[3] James A. Hunter, MD,[4] Med Bull 6(1):2–5, January 1967.

The observations of Hyman in 1932 demonstrated the feasibility of stimulating hearts to beat at a normal rate after hypoxic arrest. Weirich and his co-workers in 1957 first applied an external pacemaker to man using wires attached to the epicardium. Chardack *et al*, in 1960, were the first totally to implant an electronic pacemaker. The clinical experience at Presbyterian-St. Luke's Hospital began in May, 1961; results in the first 10 patients have been reported previously. The present report describes the results in the succeeding 60 patients who have been treated with permanently implanted electronic cardiac pacemakers.

Description of Patients**

The 60 patients ranged in age from 5 to 83 years; 43 patients were between the ages of 60 and 79. Thirty-six were male. Seven patients had evidence of ischemic heart disease manifested as angina pectoris or as one or more myocardial infarctions. In two patients complete artioventricular (A–V) block occurred at the time of cardiac surgery for a ventricular septal defect. One patient had coexistent complete A–V block and severe calcific aortic stenosis. Seven patients, all under the age of 60, had a myocardiopathy of unknown cause. Three patients required pacemakers because of paroxysmal atrial arrhythmias which alternated with sinus nodal arrest sufficient to produce Stokes-Adams episodes. Forty patients, all over the age of 50, had complete A–V block without identifiable cause; these individuals were presumed to have degeneration of the cardiac fibrous "skeleton" as described by Lev.

The reasons for pacemaker implantation were two. Two patients had intractable congestive heart failure as an accompaniment of their slow idioventricular rhythm. Forty-six patients had experienced Stokes-Adams episodes due either to abrupt slowing of an idioventricular focus or to periods of rapid ventricular tachycardia. Both congestive failure and Stokes-Adams episodes occurred in the other 12 patients.

Description of Pacemakers

The pacemakers used in this series of patients have been made at Presbyterian-St. Luke's Hospital by one of us (RWS). The basic circuit diagram has been published elsewhere. Briefly, mercury batteries supply electrical power to an oscillating circuit which permits discharge of a capacitor across the myocardium at a rate of approximately 75 per minute. Each impulse has a duration of 2 msec. and delivers approximately 10 mamp. at 6.0 volts. The electronic components and batteries are embedded in an epoxy resin which is then coated with silicone rubber.

The wires used to connect the pulse generator to the myocardial electrodes have a synthetic fiber core. Around this, four ribbons of stainless steel are wound in a helical spiral. These are soldered to platinum electrodes. The wire is enclosed in a polyethylene sheath; in turn this is enclosed in a silicone rubber tubing which is sealed to epoxy at each end.

The impulses are delivered to the myocardium by either of two types of electrodes. Fifty patients have had a left thoracotomy and pericardiotomy. For this approach, the wires terminate at epoxy covered platinum disks 9 mm in diameter. These disk electrodes are sewn to the epicardium near the apex of the left ventricle. For ten patients one wire has terminated as a platinum cylinder 6 mm in length and 3 mm in diameter. This has been inserted, under local anesthesia, either in an external jugular vein or in a cephalic vein at the shoulder. The electrodes have been advanced under fluoroscopic control into the apical segment of the right ventricular cavity to ensure good endocardial contact. With this system, the other wire terminates in a disk electrode implanted subcutaneously. The pulse generator is placed in a pocket fashioned in subcutaneous tissue overlying one pectoralis muscle with either mode of myocardial stimulation.

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TABLE 1. *Summary of Patients with Implanted Pacemakers Follow-up Period*

Type of Pacemaker	1 mo.			6 mo.			1 yr.			2 yr.			3 yr.			4 yr.		
	Dead	Alive	Pacing	Dead	Alive	Pacing	Dead	Alive	Facing	Dead	Alive	Pacing	Dead	Alive	Pacing	Dead	Alive	Pacing
Epicardial	3	47	47	2	40	39	2	31	30	1	17	17	2	4	4	1	1	1
Endocardial	2	8	8	0	6	5	0	3	3									
TOTALS	5	55	55	2	46	44	2	34	33	1	17	17	2	4	4	1	1	1
Cumulative Deaths		5			7			9			10			12			13	
Cumulative Mortality		8.3%			13.2%			20.9%										

Replacement of pulse generator units is performed under local anesthesia. The generator is exposed through a 10 cm incision, the wires are cut, and a new generator is spliced to the existing wires leading to the heart. The splices are performed with crimped connectors with a stainless steel conducting core. The splices are sealed in silicone rubber prior to implantation of the new generator.

Results

Patient Survival

Table 1 shows the status of this series of 60 patients at intervals after initial pacemaker implantation. There have been three deaths during hospitalization for implantation of an epicardial unit; one of these occurred from a coronary arterial embolus on the day after both an aortic Starr-Edwards prosthesis and a pacemaker had been implanted. One patient died of severe cor pulmonale six days after unsuccessful efforts to implant an endocardial unit. One other patient died suddenly at home two weeks after insertion of an endocardial unit. Thus, the mortality within the first month after surgery has been 8.3 percent. Two additional deaths have occurred between the first and seventh months after surgery. Forty-six were alive six months after surgery; two of these were no longer being paced, but each had fortuitously reverted to normal A–V conduction. Thirty-four patients have been followed for more than one year. Two deaths have occurred between six months and one year, yielding a cumulative survival rate of 79.1 percent during the first year of follow-up. Seventeen patients have been followed for two years and four patients for three years.

Division of patients by the period of implantation provides figures for survival comparable to the type of analysis conducted by others. Of the 24 patients who had pacemakers implanted between one and two years ago (11/1/64 to 10/31/65), 19 (20.8 percent) have survived. Of six patients whose units were inserted between two and three years ago, five are surviving (16.7 percent).

Pacemaker Unit Fate

Replacement of the pulse generator unit has become a routine procedure; no complications have occurred to the present time. No patient has undergone a second thoracotomy for replacement of a defective unit. Two patients have had either a broken wire or an abnormally high myocardial stimulation threshold, 32 and 39 months after the initial implantation respectively, and have had an endocardial unit inserted to avoid a second thoracotomy.

Forty-three instances of pacemaker failure have occurred; each has been replaced. Thus, 113 pacemaker units have been used. The reasons for pacemaker failure can be considered in three categories. The first is failure of an individual electronic component. The transformer in the oscillating circuit has failed on two occasions, six and nine months after implantation respectively. Two capacitors have changed their capacitance value sufficiently to modify the pacemaker rate four and six months after implantation. This represents a 3.5 percent incidence of component failure. Wire or electrode failure, or myocardial threshold elevation comprise the

second category. Two failures in this category have been mentioned previously. One additional failure has occurred at 14 months, necessitating the use of a subcutaneous indifferent electrode. Two of the splices made at the time of replacement have been improperly sealed with silicone rubber and have failed four and eight months respectively after implantation. This represents a 4.4 percent incidence of failure in this category. The third category is comprised of inevitable failures—that of the mercury battery power supply. Thirty-four units have required replacement because of battery failure. This has occurred between nine and 31 months (average 16 months) after implantation. Seven of these battery failures have occurred prior to 15 months and are considered to be instances of premature failure. This period of battery function which is shorter than that expected from "shelf life" studies of these batteries, is largely related to slight but harmful imbibition of water by the epoxy seal. Improved epoxies are currently under study.

The failure rate from all causes in the first twelve months has been 9 of 113 units (8 percent).

Comments

The paroxysmal hazards of acquired complete atrioventricular block have caused a high mortality rate in patients treated by drugs alone. The survival rates in the present series and in that of Chardack and his co-workers has been consistently higher.

The patient with acquired complete A–V block requires prompt therapy when Stokes-Adams episodes are occurring. At present, this therapy is best undertaken in four sequential stages. Firstly, isoproterenol given intravenously at a rate of 4 to 8 mcg. per minute will usually accelerate a slow idioventricular rhythm sufficiently to permit careful completion of the second stage. Then a temporary transvenous electrode catheter can be inserted and connected to a battery powered external pacemaker. With this in place in the right ventricle, the patient can safely undergo study and therapy of coexistant problems to insure optimal condition for permanent pacemaker implantation.

The greater simplicity and lower operative risk of the permanent transvenous approach will probably lead to increasing use as experience indicating reliability of this approach increases.

Summary

Sixty patients have been treated by pacemaker implantation at Presbyterian-St. Luke's Hospital between August, 1962 and October, 1966. The cumulative mortality figures have been 13.2 percent, 20 percent, 37 percent, and 75 percent at six months, one year, two years, and three years respectively after surgery. Nine pacemakers have required replacement after less than one year because of failure of electronic components, electrodes or wires, or premature battery depletion.

Implanted pacemakers provide an important therapeutic tool for the prevention of the sequelae of complete atrioventricular block.

(The references may be seen in the original article.)

MEDICAL ABSTRACTS

PATHOGENESIS OF VIRAL INFECTIONS OF THE NERVOUS SYSTEM

R. T. Johnson MD and C. A. Mims MD, New Eng J Med 278(1): 23–30, Jan 4, 1968 and 278(2): 84–92, Jan 11, 1968.

In 1936 Hurst's review of the pathogenesis of virus disease of the nervous system crossed the boundaries of traditional disciplines by "taking into account both the viruses and the terrain on which they manifest their activity." The concepts of neurotropism, routes of infection and selective vulnerability that he developed proved useful for many years, but recent advances in virology, anatomy and immunology make necessary a reappraisal.

Viral infections of the nervous system must now be considered uncommon but important complications of systemic infections. They can no longer be explained on the basis of rare agents with a special affinity for neural tissues, since viral meningitis and encephalitis are generally caused by common viruses. The enteroviruses (ECHO, Coxsackie and polioviruses), the agents causing mumps, lymphocytic choriomeningitis and herpes simplex and the arthropod-borne viruses have been shown to be those most frequently associated with human cen-

tral-nervous-system disease. That all these agents frequently infect man has been demonstrated by the serologic evidence of prior infection in a large segment of the population. Some of these viruses cause clinically significant disease only on the rare occasions when the nervous system is involved (for example, polioviruses and the arthropod-borne encephalitis viruses); others are a frequent cause of mild disease that assumes a more serious form when the nervous system is invaded (such as herpes simplex and mumps).

How viruses invade the central nervous system and why this invasion is infrequent are therefore problems of fundamental importance. It must be explained, for example, why a virus causing no more than a cold sore in one person can produce fatal encephalitis in another. In the past few years newer methods have made possible more precise studies of the pathogenesis at a cellular level, and data now being obtained in laboratory animals explain some of the mechanisms of viral spread and disease causation.

This review attempts to bring together these recent studies on pathogenesis and to interpret them in the light of new anatomic facts based on electron microscopy and new virologic data derived from cell-culture systems. Experimental studies using viruses pathogenic for man are emphasized, and possible correlates in human disease are discussed. An attempt is made to synthesize new concepts of how viruses spread to the nervous system, how they are disseminated within the nervous system and how infection may lead to varied clinical and pathological reactions.

KIDNEY INJURIES IN CHILDREN

T. S. Morse, J. P. Smith, W. H. R. Howard, and M. I. Rowe, J Urol 98(5): 539–547, Nov 1967.

Renal injuries in 80 children are reviewed. Injuries which involve the parenchyma alone or the parenchyma and the capsule usually require only supportive care. Those involving the blood supply or the collecting system usually require operation. Fifty-six injuries of the parenchyma with or without capsular rupture healed after supportive care without sequelae.

Injuries of the blood supply are rare. None were encountered in this series.

Two injuries involved only the parenchyma and the collecting system. One minor calyceal leak healed without operation. One major disruption required partial nephrectomy.

Fourteen injuries involved the capsule, the parenchyma and the collecting system. Despite their severity these injuries tended to be localized. Only 2 kidneys were totally shattered. A major portion of the kidney was usually amenable to reasonable efforts at salvage. Seven conservative operations were successful in preserving renal function without hydronephrosis, infection or hypertension. Four presumably salvageable kidneys were lost, two because of premature intervention and two because operation was unduly delayed. One healed without operation.

Congenital abnormalities and malignancy predispose the kidney to injury and reduce the chances for salvage. Seven children had congenital malformations, two of which were repaired, two healed without operation and three required nephrectomy. One nephroblastoma was removed. All of these lesions were entirely unsuspected before the injury.

Additional injuries were present in 40 percent of the children. Eight of the 32 children with renal injury on the left side had co-existent rupture of the spleen.

No matter how minor the trauma may appear or how obvious another injury may be, every child suspected of a renal injury deserves an accurate pyelographic study as soon after the accident as possible. An infusion pyelogram is recommended. If this is inadequate a second one should be obtained 24 to 48 hours after injury. If this is still inadequate retrograde pyelography should be performed without delay.

Studied in this manner, children with silent congenital malformations or tumors will not be overlooked. Therapy can be based upon accurate visualization of the extent of injury and the diagnosis will be established at a time when conservative operations are most likely to be successful.

HUMAN APPENDIX AND NEOPLASIA

H. R. Bierman MD, Cancer 21(1): 109–118, Jan 1968.

The relationship of previous appendectomy to cancer was studied in the consecutive postmortem records of 1,287 cases: 122 living patients with lymphomas and leukemias were also studied. Of 608 postmortem cases with cancer, 35.2% had previous appendectomy. Of a comparable group of 679 cases without cancer 24% had no appendix. The appendix had been removed in 23% of 443 cases with vascular disease; 47.9% of 94 cases with cancer of the colon and rectum (significantly at

P = <0.0001); 57.6% of 66 cases with cancer of the breast (P = <0.0001); 83% of 24 cases with cancer of the ovary (P = <0.0001); 40% of 57 patients with Hodgkin's disease and 50% of 22 patients with granulocytic leukemia. The data suggest a systemic and local effect which is exhibited only in approximately one-third of the patients with cancer, lymphoma or leukemia; they also suggest that the function of the appendix may influence the induction of leukemia, lymphoma or other neoplastic disease in a restricted susceptible population. Further prospective and retrospective investigations including animal experimentation are necessary to define the nature of this association.

DENTAL SECTION

THE "WHOLE SHIP" CONCEPT OF TREATMENT

A Fleet Preventive Dentistry Facility was officially opened on Pier 2, Naval Station, Newport, Rhode Island, on 21 January 1966. Its purpose was to serve as a central management facility in the development and testing of a more effective dental care program for destroyer personnel. This program has become known as the "whole ship" concept. It involves extremely close liaison and coordination between the fleet and shore dental facilities to achieve maximum effort and facility utilization.

Captain H. R. Superko, DC USN, Commanding Officer, Naval Dental Clinic, Newport, Rhode Island, reports that the entire crews of the last seven ships processed by this system were given a complete oral diagnosis, preventive treatment, definitive operative treatment and placed in Dental Class I and II condition to a degree exceeding 90 percent.

The Newport clinic was intentionally overstaffed to give the method a trial. After two years, the method has proven to be feasible in an area of extremely heavy dental needs where many ships without dental officers are home ported.

While the system of block appointments for those in need of dental care, as set up by Medical Department Representative, has prevailed in many areas over the years, all senior dental officers should be alert to the fact that there is a better way to accomplish the job; namely by the "whole ship" concept. The idea of a definite period when a home ported ship has "dental availability" and when virtually all dental treatment is completed for the year has proven to be highly effective.

It follows that despite dilution and turnover of personnel, the job will be easier during the ship's subsequent dental availability period. A corollary might be assumed that once fleet personnel assigned to the Newport area attain a reasonably high state of dental health, dental personnel might be reallocated to overstaff some other area for implementation of the "whole ship" concept.

Recognition of the potentiality of this method for use when and where the opportunity arises is desired. The Bureau looks with favor upon the provision of support to any enterprising senior dental officer who feels he can justify the initiation of the system in his area.

Recently the staff dental officer, CINCPACFLT, working in conjunction with the commanding officers of naval dental clinics in Long Beach and Pearl Harbor, commenced a small whole ship treatment program for mine force vessels.

As dental conditions improve under the progressive impact of both civilian and military preventive measures, similar opportunities for the establishment of the "whole ship" concept may exist in other areas.

DENTAL CORPS TRAINING

The Dental Training Committees convened in January 1968 to select dental officers for advanced training including dental internships for Fiscal Year 1969. A summary of the training recommendations is listed as follows:

1. Graduate/Postgraduate Courses (General), Naval Dental School 20
2. Graduate Course (Oral Surgery), Naval Dental School 4
3. Graduate Course (Prosthodontics), Naval Dental School 4
4. Graduate Course (Endodontics), Naval Dental School 3
5. Graduate Course (Oral Pathology), Naval Dental School 1
6. Postgraduate Level Training (Residency Type) 28

7. Postdoctoral Fellowship	31
8. Long Courses at Civilian Universities	25
9. Dental Internships	32
Total	148

Recommendations for assignment were, in part, based upon indicated preferences for training, available billets that best coincided with stated preferences, seniority as related to active duty in the naval service, academic records earned during predental and dental school training, service records, and the needs of the service.

The number of applications for graduate and postgraduate education continues to increase each year. The limited number of available billets, limited training funds, the availability of training sites with preceptors, and the needs of the service, make it impossible to fulfill all requests for advanced training.

In an effort to provide advanced training for as many junior officers as possible, the postdoctoral fellowship program was established three years ago and will provide advanced training for 31 junior dental officers in FY 1969. Additionally, the number of dental officers approved for assignment to long courses of instruction at civilian universities has been increased from eight to twenty-five in a period of two years which is a 213% expansion of this program.

It may be of interest to those dental officers who contemplate applying for future advanced training that 32% of those approved for long courses at civilian universities, for Fiscal Year 1969, had the postdoctoral fellowship accepted as the prerequisite for instruction.

The following summary of U.S. Naval Dental Corps training indicates a substantial 174% increase in long course training during the past eleven year period:

	FY58	*FY68*	*FY69*
Graduate/Postgraduate Level Training (Residency Type)	9	25	28
Dental Internships	18	32	32
Postdoctoral Fellowships	0	29	31
Graduate/Postgraduate Courses, Naval Dental School	24	32	32
Long Courses at civilian universities	3	17	25
	54	135	148

In addition, there has been a comparable increase in the continuing education program of short postgraduate courses both in-service and in civilian activities. Even with the above increase in advanced training opportunities of the Naval Dental Corps, it is regrettable that all applications for advanced training cannot be fulfilled. The Dental Training Committee strives to distribute the training assignments as equitably as possible for the overall needs of the service.

It is, and it will continue to be, the desire of this Bureau to increase the amount of training in order to meet ever increasing demands and to reflect the highest degree of professional excellence attainable for the benefit of all Navy and Marine Corps personnel.

All applicants for advanced training commencing in Fiscal Year 1970 are requested to submit applications to the Bureau of Medicine and Surgery at least six weeks prior to the deadline of 1 December (MMD 6–130) to allow sufficient time for processing of records.

In conjunction with applications for assignment to any long courses of advanced training, applicants are requested to comply with the recent (CH–40) MANMED ART. 6–130.

The following discrepancies were common in the FY 1969 applications:

1. Failure to have both predental and dental school transcripts forwarded. Art. 6–130(2)
2. Failure to indicate a first and second choice of desired training (if appropriate). Art. 6–130(4)
3. Failure to submit the correct training agreement. Art. 6–130(5)
4. Failure to submit applications at least six weeks prior to the deadline of 1 December. Art. 6–130(1)
5. Failure to specify the course desired at the Naval Dental School, National Naval Medical Center, Bethesda, Maryland. Art. 6–130(4) (a).

In order to insure prompt processing of applications and to save extra correspondence, all applications must be in accord with MANMED Art. 6–130.

SPECIALTY TRAINING IN ORTHODONTICS

Relative to the changing dental standards of candidates for the Naval Academy, Naval Reserve Officers Training Corps programs and increasing pressures to continue limited orthodontic care for dependents at certain overseas bases, a long course training program at civilian universities has been established in the specialty of Orthodontics, (*U.S*

Navy Medical News Letter, Vol. 50, No. 9, 3 November 1967). Due to limited funds, only one dental officer was approved for a long course of instruction in Orthodontics commencing in Fiscal Year 1969.

Applications for training in Orthodontics commencing in Fiscal Year 1970 will be considered. This is a keenly competitive field and the program will be limited to a very few dental officers.

Accordingly, it is suggested that those applying for Orthodontic training indicate a second choice of desired training.

Applicants must be in the grade of lieutenant or lieutenant commander and have completed a tour of duty at sea or in areas considered foreign shore for rotational purposes. The prerequisite of a Postdoctoral Fellowship or Graduate Course, Naval Dental School, may be waived for outstanding applicants for instruction in Orthodontics.

NURSE CORPS SECTION

THE CLINICAL SPECIALIST

The Clinical Specialist was the topic of a paper presented by Mrs. Louise Anderson, Nurse Director, at the Nursing Section of the Association of Military Surgeons annual 1967 Convention. Mrs. Anderson's paper is presented here for our readers.

The truly professional nurse functions in the area of judgment and decision. She must constantly evaluate the patients with whom she deals and adjust her manner, approach and demeanor to the individuality of the patient with whom she comes in contact. The success or failure of this person in the hospital setting appears to me to rest not only on the knowledge and the skill she brings to the clinical situation but also on the degree to which she gives herself. I am not talking about dedication but rather, I think, attitude. For some time the administrative staff with whom I work has considered the many aspects of professionalism in the hospital setting for the reason that demands for nursing service are increasing, the available knowledge for applications to the recovery of the patient is extensive but the quality of patient care deteriorates for lack of sufficient skilled personnel to administer care. This is a serious problem which cannot be solved with the traditional methods dependent upon sufficient personnel to carry out ever-increasing techniques.

In 1965 the administrative group to which I referred before, decided that we needed a truly professional nurse to carry out three functions:

1. To demonstrate the value of knowledge, skill and attitude blended together in the solving of nursing problems related to the complicated patient.

2. To set an example and to interpret through cooperative effort the quality of care required for the patient in a clinical research setting.

3. To make the time of the expert nurse available to solve the problems of nursing related to research protocols by being available to the research physician upon his written request.

Our concept of this nurse's function was not too clear but we knew that she must have freedom of movement, flexibility of schedule, and the authority to make professional decisions which would be final in the sphere of her operation.

We recognized that the sabotage of this position was possible by the head nurse, the staff nurse, or even the physicians she was intended to assist. With this in mind we began an interpretive program of the position we envisioned but could not name. From all categories of nursing personnel we received questions and suggestions which were very helpful in clarifying some of the details of relationships which could have made for failure had they gone unnoticed.

By September of 1965 we had developed a job description and secured a rating which placed the position at the same grade as a head nurse. Our criteria for selection was quite simple:

1. The candidate for appointment must have demonstrated with at least one year in the staff nurse position the ability to give superior nursing care in a selected category of patients (for example, cardiac, neurological, cancer, etc.).

2. The individual must have demonstrated an understanding and acceptance of those components which make for professional responsibility and professional performance.

3. The individual must have demonstrated a flexibility and an interest in direct patient care which would serve as an example to associates in the clinical situation.

4. The candidate must have demonstrated personal and professional integrity in relation to nursing as a whole.

Eight nurses were originally appointed to the position which we call clinical expert, and the process of developing a place in the nursing structure began. The way in which the clinical nurse expert functions has been quite consistent from the beginning. The nurse in this position is assigned to a nursing service and works out of the office of the Chief, Nursing Service. Her service is obtained by requisitions originating with the head nurse of a nursing unit. The clinical expert must then assess the situation and decide where she is most needed. She may split her time between two units but wherever she works her main function is the solving of nursing problems. If patient care appears to be the most important request, the clinical nurse expert works out a schedule for the patient, gives the direct care, evaluates the personality traits of the patient, and attempts to establish a high level rapport with the patient. Having worked out these areas the clinical expert nurse is then obligated to communicate her solutions to the total staff. The interpretation may take place in a team conference or, if the patient has many complex procedures or personality problems, the clinical expert may ask individual staff members to work with her over a period of time to demonstrate the most efficient use of time in caring for the patient.

It is the responsibility of the clinical expert to schedule herself at the time she is most needed on the service. She works a 40-hour week but she may work four hours one day and ten the next if she thinks this is indicated. The concept of this position as established at the Clinical Center is the development of a professional individual who has skill in evaluation of patient needs, interpersonal relations, and who demonstrates mature and professional judgment in making decisions.

Traditionally, nurses have progressed by way of the administrative ladder which is somewhat illogical when one considers the real function of nursing and the pressing need for quality patient care in today's society. The eight nurses appointed as clinical experts were well aware of their responsibility for demonstrating the value of the clinical expert in direct patient care and for establishing a pattern which would allow for promotion in the patient care area of clinical practice. We felt this was an opportunity for those nurses who went into nursing to take care of patients and whose only satisfactions were derived from this line of endeavor.

It is implicit in this position that concentration of time is in the area of patient welfare and no administrative responsibility may be imposed. Further, there is danger of misinterpreting this position with that of a senior staff nurse and the two positions are distinct.

The establishment of a new concept is always difficult and especially so in a profession which has the background of tradition that nursing has. However, in two years we have seen an influence by the nurse experts which has been beneficial for patients and personnel alike. Most important, perhaps, is the reduction in post-surgical complications, which we cannot actually measure, but which is observable in the areas where she functions. We attribute this reduction to the security experienced by the patient who is prepared for surgery both physically and emotionally and who develops confidence in a single individual who takes time to know him as a person with a personality distinct from all other patients. This patient then is likely to be less anxious and less tense which certainly is desirable for a surgical patient. Secondly, there appears to be a marked improvement in relationship with physicians responsible for patient care. The fact that a nurse may provide time for discussion and mutual planning with physicians for as long as necessary without having to consider an assignment which goes undone makes for a greater ease in free discussion and solves problems by early cooperation in planning new protocols.

Further, with improved communication and interpretation of goals in specific research projects several of the clinical experts have designed equipment to facilitate the accomplishment of the goal.

The expectation of a good role model has developed in much the way we hoped it would. The clinical expert who orients new personnel to patient care only relates as a co-worker and plans to spend sufficient time to interpret, encourage, and evaluate the nurse who is new in the clinical research setting. There is a peer relationship which makes for easier communication than that of supervisor to employee. In addition, the head nurse seldom has time to spend in proper orientation and the need for haste reduces the possibility of full understanding on the part of the new employee. The clinical nurse expert provides times to know a new nurse and can frequently allay fear or misunderstanding by communicating her needs to the head nurse or supervisor.

As previously stated, it is the responsibility of the clinical expert to plan her own schedule in rela-

tion to the needs of the service where she is assigned. It is not uncommon for the clinical expert to plan to work with a young nurse for three or four nights when she is first assigned to night duty. The very fact that such assistance is available appears to make a great difference in the security and degree of confidence with which the nurse performs.

The clinical experts meet together once a month for group discussion and analysis of their activities. The Chief, Nursing Department, may meet with them, but not always. It is the responsibility of the group to make suggestions for expanded functioning and to constantly evaluate the nursing care of patients as they see it given. Over the two-year period there has been a noticeable change in the emphasis on activity. Originally, the requested considerations were more in the direction of patient care. At the present time there seems to be a greater need for orientation of personnel but this could change overnight. Suffice it to say that we feel this position holds much promise for the accomplishment of a high quality of patient care, for the development of the nurse as a truly professional practitioner and for greater satisfaction of nursing personnel in the work situation.

We have had evaluation sessions by the senior administrative group and by the head nurse group as well as by the staff nurses and all were enthusiastic. We are cautiously optimistic in terms of what this can mean for the best utilization of nursing knowledge and nursing time, and to date we are honestly pleased with our experiment.

FIVE NURSE CORPS OFFICERS SELECTED AS OUTSTANDING YOUNG WOMEN OF AMERICA

The below named five Nurse Corps officers were selected for inclusion in the forthcoming publication of *Outstanding Young Women of America.*

LT Shirley Ann Hill, NC USNR
LT Leanna Jean Crosby, NC USN
LT Rosemary B. Geraghty, NC USNR
LT Mary Lou Taylor, NC USN
LT Caroline Luisa, NC USN

All of the above Navy nurses were assigned to the USS Hospital Ships serving in Vietnam.

The purpose of the publication of *Outstanding Young Women of America* is to recognize and honor the truly outstanding young women of the USA by focusing attention on their capabilities and capacity for progressive activities. Selections for this publication were made by local women's clubs throughout the United States, college alumni associations and military services.

OCCUPATIONAL MEDICINE SECTION

ASBESTOS AS AN ENVIRONMENTAL HAZARD

Irving R. Tabershaw, MD, Berkeley, Calif., JOM 10(1): 32–37, January 1968.

You have heard today that in industries using asbestos as a basic material, that is mining, milling, fabrication and installation, that a relationship has been established between asbestos exposure and fibrosis of the lung, lung cancer, and possibly with an increase in the incidence of mesothelioma and gastrointestinal malignancies. The incidence and severity of the pulmonary fibrosis (asbestosis) are apparently dependent on dose. This dose-response relationship in asbestos workers will probably be proven in time to be true also for the neoplasia of the lung, pleura and gastrointestinal tract. Concern, however, has been expressed that asbestos in ambient air may constitute a real threat to the entire public and not just to those occupationally exposed.

This grave implication is summarized in an article by Thomson, who raises the question of "whether a small amount of asbestos in the lung bases or in the adjacent pleura or peritoneum is an effective carcinogen or co-carcinogen in humans, if it is present there for 30 years or more." This concern is reiterated by Selikoff and his co-workers in a lengthy editorial with the statement: "The neoplasms now encountered associated both with industry and environment are consequent upon inhalation of asbestos associated with the limited asbestos production of some 30 years ago. The neoplasms

associated with current utilization and exposure to asbestos will not be evidenced until 1990."

If this is true, it changes the order of magnitude of the hazard and places asbestos in the forefront of public health problems.

The data which lead to this speculation is mostly epidemiologic in character. There is unequivocal evidence that fibrosis of the lung (asbestosis) occurs in asbestos workers. Pleuritis is a frequent sequela of asbestos exposure and a rare malignancy of the pleura, mesothelioma, shows a remarkable increase in asbestos workers and in individuals living near asbestos-producing mines and factories. Neoplasms of the lung occur more frequently in individuals who have asbestosis or who are occupationally exposed to asbestos.

These findings, per se, would not lead to the sweeping speculations made by Thomson, Selikoff and others were it not for the additional finding that a large percentage of individuals over the entire world show "asbestos bodies" in their lungs at autopsy even though most have had no known occupational exposure to asbestos. Since "asbestos bodies" are specific for past exposure to asbestos or similar fibers, the speculation that all of us are under some increased threat of lung cancer due to the presence of ambient asbestos is valid.

Assessment of the magnitude of this threat is the crucial question. Forces such as the increased use of asbestos products and the general soiling of ambient air in our industrial technological society demand that we make some judgment now. If we cannot make this determination, we must direct our research into those channels which will be most likely to give us early and definitive proof.

Epidemiological studies are of prime importance and in fact present the most convincing evidence that asbestos may be dangerous to the working population, but the likelihood of proving that there is an increased risk to the public from asbestos in ambient air, by using epidemiologic methods, is very small. Even if all the factors which could influence its evaluation are known and a prospective study devised to demonstrate an effect by 1990, any conclusions from such a study would be subject to severe doubt because of the many variables which could not be controlled satisfactorily.

The experimental approach can provide only tentative answers since it has been demonstrated that, while asbestos will produce irritation, plaques and malignancies in serious cavities, it is relatively inert as an over-all irritant to biologic materials. Furthermore, the translation of effect from any species of animals to man is difficult at best and is made even more questionable by marked variations in respiratory tract response by different animal species. The animal selected must most nearly resemble the human lung in order for the experiments to be meaningful.

Exposure factors are not completely understood. Asbestos is said to be indestructible, but the term is a relative one; high heat, chemicals and body fluids produce changes in its physical and chemical properties in time. There is undoubtedly a difference in effect from a heavy, brief or continuous exposure as occurs in industry to sustained minor exposure which may occur from ambient air pollution. Selikoff has iterated many times that there is an increasing use of asbestos and surmises that we are presently seeing lung malignancies "consequent upon inhalation of asbestos associated with the limited asbestos of some 30 years ago." The implication is clear that if his relationship (tons of asbestos produced to incidence of lung malignancy) is true, the multifold increase in its use has started an upward trend which will be reflected for the next 30 years and more. This extrapolation is unwarranted.

Increased production cannot be equated with increased hazard, especially in a substance like asbestos which is used for the most part in products which are unlikely to become airborne. The largest amount—one can only guess at the percentage—goes into asbestos products which, once applied do not disintegrate, such as building materials and floor tile. A fair estimate might be that some 10 to 15% of the asbestos in the approximately 3,000 end-products containing this mineral, e.g. brake lining and asbestos textiles, may be deterioration, weathering, heating, etc., become airborne. However, there are no studies of asbestos concentrations in ambient air. Indications that asbestos may be carried considerable distances in the airstream are based upon: (1) Analysis of deposits on the surface of the earth, snow, etc.; (2) evidence that significant numbers of people with mesothelioma worked or lived near asbestos mines or plants; and (3) evidence that a significant population has asbestos bodies in their lungs at autopsy. But as yet the type, amount and particle size of ambient airborne asbestos has not lent itself to systematic detection and identification. It should also be borne in mind that asbestos deposits have mineral outcrops and hence there is a strong possibility that asbestos in ambient air may be a natural phenome-

non and not only a result of increased industrial activity.

Clinical experience indicates that the appearance of asbestosis (pulmonary fibrosis) is dose-dependent. Children have died of asbestosis and cor pulmonale after a few years of an overwhelming exposure. Sluis-Cremer gives an average in one factory in South Africa of 6 years at work before asbestosis was manifest. Jacob and Anspach, in Dresden, determined an over-all average of 30 years before the asbestosis became disabling. X-ray changes are induced in most cases after 20 years' employment as an insulator. One of our cases showed evidence of the fibrotic process on lung biopsy some 22 years after a heavy exposure of less than 2 years' duration.

While long latency is usual and progression of the fibrotic process may continue long after the exposure has ceased, there is little information forthcoming regarding quantitative data on the dose which each individual was exposed to. Lung clearance studies indicate a marked difference in the effects of short, heavy dust exposures as compared to minor, low exposures. Heavy dust inhalation incites an acute flammatory reaction and stasis in the respiratory bronchiole and adjoining alveolar ducts and may provide a nidus for a continuing effect.

That asbestosis, i.e. the pneumoconiosis, does not present a major problem for the future is mostly due to the fact that the occupational population at risk, which is difficult to determine exactly, is still quite small and can never reach large numbers.

While members of the construction industry, for example plasterers and some automobile workers, e.g. brake repairmen, may have greater exposures than insulators working directly with asbestos products, it is safe to say that the kinds of exposure experienced in industry will never affect any sizable group in the general or working population.

The threat from asbestos, however, lies in its possible association with lung cancer; and the expectation that there will be no increase in the mortality from this disease among exposed workers is not so sanguine. Cancer of the lung occurs more frequently in those with occupational exposure, whether or not they develop fibrosis, and this evidence is amply substantiated. Two aspects are not known, the pathogenic factors and the dose of asbestos which produce this increased susceptibility. We do not know whether asbestos has properties of primary carcinogenicity or whether its effect is entirely synergistic.

A dose too small to produce fibrosis, i.e. asbestosis, may, nevertheless lead to lung cancer. A dose large enough to produce asbestosis may cause malignancy if the worker does not die first from his pneumoconiosis. However, many men, after a lifetime of work with asbestos products—specifically insulators—show no evidence of any untoward pulmonary pathology. Again, in all of these, the amount of asbestos inhaled is unknown. When the dose is known to be related to the incidence and severity of a disease (and it grossly appears to be the case in asbestosis), it is safer to postulate that a non-threshold relationship exists. From a practical standpoint, however, asbestos would be an unusual disease agent if it did not have such a threshold.

Our findings support those of other investigators who state that pleuritis occurs in about 25% of insulation asbestos workers. The incidence of mesothelioma in this group is extremely large, considering the rarity of the tumor. Selikoff reporting on a series of 124 deaths from neoplasia in insulators found 10 with mesothelioma. This malignancy has also occurred in increased incidence in some populations which did not work directly with asbestos. In a very large proportion in South Africa and in a considerable number of the victims of this malignancy in the United States, environmental exposure is postulated as the cause since they lived close to asbestos plants using especially amosite or crocidolite. The evidence is strong that the source of the agent was indeed airborne from the asbestos factories or mines, even though many of these individuals did not show an underlying asbestotic fibrosis. However, the ambient concentration or indeed the specific type of asbestos to which the person was exposed and which could be responsible for the disease has never been determined, either in the neighborhood or in the working environment.

An increased incidence of gastrointestinal malignancy is still being investigated, but the statistical inference is strong that there is an increased susceptibility in those exposed to asbestos. This will probably be clarified in time. Emphysema or chronic bronchitis, if it does occur as a result of inhalation of asbestos dust, would always be obscured by the underlying pneumoconiosis; and the diagnosis of these conditions would always be considered a secondary rather than a primary disease.

A link and perhaps the key to the problems lie in understanding the role of the "asbestos body" in the pathogenesis of the different tissue responses. Our experience supports the statement of Gough:

"Asbestos is diagnosed histologically by the association of asbestos bodies and asbestos fibers with fibrosis." However, what the "asbestos body" means in individuals who apparently have never been exposed to asbestos is not clear. If this can be explained, inferences then could be made with some certainty regarding the potential environmental hazard.

The presence of "asbestos bodies" in the lung is a biological indicator of exposure to asbestos. Whether or not other mineral fibers can produce an "asbestos body" is not pertinent in an environmental sense. The highest concentration of mineral fiber in ambient air is overwhelmingly asbestos and hence one can assume that "asbestos bodies are almost entirely derived from asbestos fibers." "Asbestos bodies" probably can be found in every lung at autopsy if searched for long and hard enough and an occasional one is adventitious and simply indicates that mineral fibers make up a part of the dust in our environment.

The fibrosis of asbestosis is nonspecific and has no special structural characteristics except for the presence of "asbestos bodies." Hence, interstitial fibrosis without the presence of "asbestos bodies" cannot be called asbestosis. Conversely, however, "asbestos bodies" in sputum or lung tissue without fibrosis is not asbestosis but simply an evidence of exposure. Phagocytosis by macrophages is a major cleansing mechanism of the lung; they engulf the offending mineral fiber producing the typical "asbestos body". No relationship has been established between the number, type, or size of "asbestos bodies" and the time of exposure, fiber size, concentration, or form of asbestos.

Individuals who show "asbestos bodies" on lung smears at autopsy do not seem to have an increased incidence of any specific pulmonary disease. "Asbestos bodies" may be found in lung smears and not in the correlating tissue. Cauna et al. found that only 4% of lungs showed "asbestos bodies" on histological section, whereas smears of the same lungs showed "asbestos bodies" in 41%. Our findings are similar—lung smears in consecutive autopsies without known exposure to asbestos revealed an incidence of "asbestos bodies" in 45% while search of the matched lung tissue yielded only 3%. This may be a function of the amount of material available for study since the lung smear represents a much greater anatomic area than the lung tissue studied in histological section.

Our own interpretation is that while the differences in amount of material which is available for study may account for some of the disparity, there is evidence that mineral fibers are cleansed through the macrophage system and hence found in the alveoli and bronchial lumina but do not enter into the interstitial tissue. Only overwhelming exposure or perhaps some other factors which permit fibers to penetrate with formation of interstitial "asbestos bodies" lead to lung malignancy, pleuritis and mesothelioma. "Asbestos bodies" are not seen frequently in routine histologic study of lung pathology.

Our present view is that asbestos fibers are phagocytized in the airways and excreted in the sputum. In some instances the fibers penetrate the bronchial tree, giving rise to fibrosis, or into the pleura producing pleuritis. Co-factors, which are not completely understood at present, operating with the asbestos cause an increase in lung cancer susceptibility and in the appearance of mesothelioma. As the role of the "asbestos body" becomes clearer and more data becomes available on the distribution, type, fiber size, and concentration of airborne asbestos and the role of co-factors, the better we will be able to assess the potential environmental hazard from this ubiquitous mineral.

In summary, if one accepts the assumptions (1) that asbestos minerals increase the risk of lung cancer in occupational groups, (2) that they lead to an unusual risk of mesothelioma of the pleura and peritoneum in occupational groups and those living near asbestos plants, (3) that such malignancies usually result from exposures 30 to 50 years earlier, (4) that the "asbestos bodies" found in from 25 to 50% of lung smears from routine autopsies are probably due to asbestos in most cases, (5) that these "asbestos bodies" may result from recent exposures as well as those many years earlier, (6) that world production and use of asbestos has increased from 500,000 tons to 3,500,000 tons in 30 years, it is important to consider whether or not asbestos is a major threat to public health. One is not yet justified in such a conclusion, in view of the fact that much of the world tonnage goes into uses that do not lead to air contamination; asbestos is not actually indestructible, that the effects are dose-dependent, and that low doses probably lead to lower rates and long latency.

Nevertheless, there is need for epidemiologic studies directed to groups with intermediate exposures and for evaluation of the beneficial effects of cessation of smoking. Another need is for experimental and industrial hygiene studies to determine the nature and degree of exposure. Biologic

studies centered on the meaning of the "asbestos body" are crucial to understanding the clinicopathologic response. Strict control of industrial and neighborhood environments is essential, but it is premature to extrapolate from the effects of heavy exposures to minor and low level exposures.

(The references may be seen in the original article.)

INDUSTRY'S NEW PLAGUE: PULMONARY DISEASE

Joseph C. Fagan, Chairman, Dept. of Industry, Labor & Human Relations, State of Wisconsin Safety Maintenance pages 37–40, February 1968.

Five years ago, the words pulmonary disease would have brought to mind such occupational diseases as silicosis, asbestosis, tuberculosis. Today, we have to consider the broader term respiratory infections, not elsewhere classified because of our present inability to separate the respiratory infections, caused by the new chemicals and processes, into neat categories. For example, we have the relatively new problem of TDI (toluene diisocyanate) which affects various parts of the respiratory system—sometimes it strikes the nose and throat, sometimes the bronchial tubes and/or lungs, and sometimes it involves the entire respiratory system.

First, let's consider the older, better known pulmonary diseases. In Wisconsin, the law bringing occupational diseases under our Workmen's Compensation Act became effective in 1919. The single most costly occupational disease in Wisconsin has been the pulmonary disease known as silicosis (we include silico-tuberculosis in this category). From 1919 through 1966, over 900 silicosis claims have been adjudged compensable or approved as compromises, with total indemnity and medical expenses of almost seven million dollars.

The spate of silicosis and other occupational disease claims during the depression period, although costly, created an awareness of occupational diseases. This resulted in substantial efforts to control the known hazards. Plant sanitation and medical check-ups became commonplace. In Wisconsin, we have now reached the point where we stress 90 percent education and only 10 percent enforcement.

The other major pulmonary diseases that crop up in our workmen's compensation statistics are tuberculosis, pneumonia, pneumonitis, asbestosis and pneumoconiosis (not elsewhere classified).

Our statistical history of tuberculosis as an occupational disease goes back to 1919. There have been no significant variations in the number of cases from year to year. Most of the cases have been incurred in hospitals and allied health services. Two hundred claims have been compensated through 1966, with indemnity and medical costs of over $700,000.

For the other four pulmonary diseases referred to above, our statistical history covers the years 1937 through 1966. The number of cases compensated and total indemnity and medical aid were, respectively: pneumonia, 37 and $32,767; pneumonitis, 19 and $6,319; asbestosis, 11 and $198,784; pneumoconiosis, not elsewhere classified, 8 and $65,098.

Considering all pulmonary diseases discussed above, the total known number of cases was over 2,000; total known indemnity and medical costs, almost eight million dollars. Silicosis accounted for almost 46 percent of the cases and over 84 percent of the indemnity and medical costs.

The above sounds like a small amount when one considers that in Pennsylvania, where miners disabled by pneumoconiosis are paid from state funds, payments in fiscal 1966 totalled over 27 million dollars.

The common hazards of silica dust and asbestos are pretty well known. However, how many are prepared to measure exposure to crystalline free silica which may be used rather incidentally in an operation at a plant that is not normally considered to be a dusty industry? Silica flour is used, for example, as a filler in some paint mixtures.

Talc and soapstone powders have been found to produce disabling pneumoconiosis in lesser concentrations than dusts made up of silicates, with the result that no more than 20 million particles per cubic foot of air is considered safe. These two materials often have some quartz content, sometimes as much as 20 percent; thus exposure should be limited to 10 million particles per cubic foot of air.

What about those respiratory infections, not elsewhere classified by our Statistical Division? From 1937 through 1966, over 800 cases cost almost a quarter of a million dollars. The majority of the claims arose from contact with toxic and noxious substances, such as dusts and chemicals.

It will be a different story from now on. We have a backlog of unsettled cases which are costing in the millions of dollars—one self-insured employer, alone, has paid out more than one million dollars. It is almost impossible to pinpoint in every case the exact part of the respiratory system involved; we do know that, in many of the cases, the physicians are seeking to find out the long-term effect on the lungs.

New chemicals and processes have brought about this situation. Silica and asbestos have long been recognized as cripplers and killers; but who, five years ago, would have been prepared to listen to a discussion of epoxy resins, methyl ethyl ketone plasticizers, toluene diisocyanate (and other tongue twisters), in conjunction with pulmonary diseases?

The incidence of silicosis was traditionally limited to a relatively few industries and occupations—in fact, in some industries a hacking cough was a sign that a man had a job. The new hazards can be found in almost any industry, in almost any occupational classification—yes, even in the home. Progress is wonderful, but the exotic new chemicals and powerful new pesticides are endangering the health—and the lives—of many of our workers, both on-the-job and off-the-job.

For the past few years, an extensive study has been carried out by two physicians from the University of Wisconsin Medical School; Dr. Louis W. Chosy, Instructor of Medicine and Dr. John Rankin, Professor of Medicine. A National Institutes of Health grant supports their research. Working closely with affected Wisconsin employers, they have personally treated several hundred cases involving respiratory conditions resulting from exposure to glues, insulators, adhesives, foam plastics, etc.

As explained by Dr. Chosy, "These resinous compounds have been developed by modern chemistry. Chemically and simply speaking, scientists developed the new compounds by adding different chemical ingredients to a basic polymer molecule under varying conditions. The materials are highly reactive only while they are first being used. After a glue dries, it is no longer reactive and therefore causes no one any trouble. There are many industrial uses of the new compounds. They are used, for example, in adhesives which can bind metal or effectively encase electrical circuits."

"In almost every case studied," said Dr. Chosy, "the affected persons' ailments were initially diagnosed as sinus trouble, pneumonia, chronic bronchitis, or asthma—all of which may be side effects of exposure to polymer compounds. With added exposure, respiratory problems may become more severe, resulting in ear infections, sinus inflammation, or bronchial pneumonia. The full range of exposure effects is not completely understood. The best treatment for exposure is to keep away from the compounds. This poses a special problem for the workman whose job requires contact with resinous materials. And complete recovery may require prolonged absence from exposure. And, re-exposure, even after 'recovery' starts the problem over again, often quicker than the first time."

"These polymers may be encountered by the scientist in his electronics lab, the laborer in a lumber mill, the sportsman repairing his fiber glass boat, or even the captive husband painting the house," he said.

"Largely," said Dr. Chosy, "the answer is education in the dangers of indiscriminate use of these adhesives and resinous compounds as well as urging industry to give closer attention to the potential medical problems of their workers. In well-ventilated plants where resinous compounds are used, workers usually are not affected. Contact with these new materials could conceivably become an increasing problem for the man on the street. These compounds are used in a variety of products—such as epoxy paints, enamels, lacquers and glues—primarily designed for home use."

Our safety inspectors have also been working closely with some of the employers who have had the misfortune of using a chemical process without understanding the medical problems that would ensue. We try to work with the employer to help him solve his problems.

Our largest workmen's compensation insurance carrier has set up an industrial hygiene laboratory equipped with the latest devices used in chemical analysis. Their industrial hygienist collects air samples with a midget impinger, which pulls a measured volume of air through a chemical solution that traps TDI fumes. TDI, an ingredient of the polyurethane foam, can produce respiratory symptoms in very small atmospheric concentrations. He measures the intensity of the dye's color by using a visible light range spectrophotometer, which determines what percent of a beam of light is trans-

mitted by the dye solution. This is an indicator of the concentration of TDI in the solution.

Our workmen's compensation records show that quite a few Wisconsin employers have become aware of the problems of certain new production processes and have corrected the processes. In these plants, the affected workers were given the choice of staying at their old job or transferring to a different part of the plant—many transferred. Some sought jobs elsewhere, on advice of their physicians. Some are still being paid workmen's compensation. We have had cases where a worker who has transferred to another part of the plant comes in contact with others who are working with the "clean" process—in lunch rooms, etc.—and becomes disabled again. Once felled by TDI, some affected workers cannot stand a whiff of it; one such employee has claimed that other workers bring it out on their clothes and back come her old difficulties.

Not enough physicians are aware that these new materials are causing respiratory problems. If a given physician sees only isolated cases, he is apt to consider his patient's illness as a chronic one, rather than one due to his work.

At the present time, it is not always possible to determine from the label whether or not a potent sensitizer, a corrosive, a primary irritant, or a harmless substance is included in the product. How much does it mean to the ordinary user to read on a label: "Use in a well-ventilated area". At home, or in a small plant, one would think it enough to open a few windows and place a few fans around. Where is the warning that the products can cause respiratory difficulty or dermatitis?

Unless warnings and precautions are clearly stated on labels, the manufacturers and, under some conditions, the sellers of proprietary chemicals are liable for injuries and property damage that result from their use. However, this means little to the worker who is disabled or fatally injured through improper use of a chemical—improper use because the label did not state clearly what precautions should be taken.

But, we must face the fact that the potential threat to the health and well-being of our workers has never been greater. Although industry is spending unprecedented amounts of money to protect its employees from all known hazards, today's technological advances are creating problems faster than we can handle them.

EDITOR'S SECTION

CAFFEINISM

A CAUSE OF LONG-CONTINUED, LOW-GRADE FEVER

Hobart A. Reimann, MD, JAMA 202(12):131–132, Dec 18, 1967.

Low-grade irregular fever, insomnia, anorexia, and irritability affected a psychoneurotic woman for months. She habitually drank an excessive amount of coffee. Fever and the symptoms disappeared after the intake of coffee was reduced. Fever is one of the manifestations of caffeinism.

The excessive use of common household items including sedative drugs, cigarettes, alcohol, tea, coffee, dentifrices, and even peanuts can induce illness mistaken for other disease. The cause is easily overlooked unless a patient's habits are discovered. Prompt recognition obviates much clinical effort, laboratory testing, unnecessary therapy, and expense. Removal of the cause is the cure.

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Report of a Case

A housewife, aged 39 years, complained of having a "cold" for six months because of almost daily low-grade fever with occasional flushing and chilliness, insomnia, irritability, anorexia, loss of 20 lb (9.1 kg) of weight, and conjunctival irritation. Cramps in the epigastrium and of the toes and cold hands and feet occurred at times. The oral temperature in the daytime usually rose to 99 F (37.2 C) or more, and occasionally to 100.4 F (38 C).

Phenobarbital was taken nightly to induce sleep. Five abdominal operations had been done during 20 years, and menses ceased after total hysterectomy in 1963. She has two healthy children. Three genetic relatives have diabetes.

In June 1967, after detecting leukocytes and albumin in a sample of urine, probably not collected with proper care, her physician suspected pyelonephritis, possibly as a result of ureteral obstruction from scar formation after the numerous surgical procedures. The patient never had dysuria. No other abnormalities were found on physical examination nor in laboratory studies. Because antimicrobic therapy failed to influence the temperature and the symptoms, the patient was sent to the hospital for investigation.

On admission at 4 p.m., her oral temperature was 99.4 F (37.5 C); pulse rate, 100 beats per minute; respiration rate, 18/min; and the blood pressure, 120/80 mm Hg. She was apprehensive, pallid, and weighed 107 lb (48.5 kg). No abnormalities were evident on physical examination. The extremities were cool and dry, the reflexes were normal, and there was no tremor. Conditions for diagnostic consideration were, among others, pyelonephritis, diabetes, hyperthyroidism, tuberculosis, lymphoma, psychoneurosis, habitual hyperthermia, and factitious fever.

During five days in the hospital, no fever occurred. Rectal temperature averaged 98.8 F (37.1 C); the highest temperature on two days was 99.8 F (37.7 C); the lowest, 97 F (36.1 C). Oral temperature was 0.5 to 1 F degree lower. The pulse rate fluctuated between 70 and 100 beats per minute, averaging 80 per minute. The blood pressure declined to 105/60 mm Hg.

Daily urinalyses disclosed no abnormality, except on one occasion a trace of albumin and a few diphtheroid bacilli were found. Urine cultures remained sterile. An intravenous pyelogram showed no lesion in the kidneys, ureters, or bladder. Two fasting-blood-sugar determinations revealed 90 mg/100 ml and 102 mg/100 ml. Two two-hour samples of blood contained 251 mg and 173 mg of glucose, respectively, but glycosuria was absent in ten samples of urine tested during three days. A roentgenogram disclosed no pulmonic infiltration, and dermal tests with tuberculin, histoplasmin, and coccidioidin were nonreactive. The hemoglobin value was 13.8 gm/100 cc; the leukocytes numbered 8,800/cu mm with normal constituent cells.

Thus far, none of the data gave clues to the cause of fever, loss of weight, insomnia, and albuminuria. The patient has a compulsive personality but denied that social, economic, or other factors would account for emotional disturbance. Habitual hyperthermia or factitious fever are not accompanied by loss of weight or insomnia. Normal hyperthermia related to the menstrual cycle was not likely after menses ceased in 1963.

On further inquiry, the patient stated that she worked as a waitress from 5 p.m. to 11 p.m. During the day she smoked a pack or more of cigarettes and drank from 15 to 18 cups of brewed coffee from 8 a.m. until 4 p.m. when she left home for work. Oral temperature, measured at times by the patient's physician, at times by me, and four times a day by her, usually exceeded the norm and occasionally rose to 100.4 F (38 C) only between noon and late afternoon. This behavior, the normal temperature observed in the hospital where only one cup of coffee a day was served, and the symptoms suggested caffeinism. The response to caffeine begins from 30 to 60 minutes after ingestion and persists for several hours, which is consistent with the patient's daily timed appearance and disappearance of fever.

The patient had no withdrawal symptoms after the intake of coffee was restricted. Usually, headache and lassitude ensue a few hours after deprivation of the accustomed amount in habituated persons. The temperature remained normal, appetite improved, insomnia lessened, and she regained 5 lb (2.3 kg). The patient declined a request to resume the former high intake of coffee to see if fever again appeared.

Effects of Caffeine

An ordinary cup of coffee contains about 0.1 gm of caffeine. Accordingly, the amount ingested by the patient in 15 to 18 cups was between 1.5 gm and 1.8 gm or about 36 mg/kg. A single 1-gm dose of caffeine causes mental confusion, shivering, tremor, tachycardia, vomiting, and diarrhea, but the patient's intake was extended over a period of eight hours. A large therapeutic dose is 0.25 gm, and 10 gm is said to be fatal. Caffeine is diuretic, rapidly metabolized and excreted. Excretion of large amounts may be delayed, but it is not cumulative.

In experimental studies, one hour after 0.5 gm of citrated caffeine was given, the temperatures of three persons rose 0.4 F, presumably as a result of stimulation of the hypothalamus. Amounts of 0.25 gm to 0.4 gm given before retiring increased temperature and mobility at night. Aminophylline

(theophylline ethylenediamine) poisoning in children caused hyperpyrexia and albuminuria. The basal metabolic rate increased from 7 percent to 23 percent after the ingestion of 0.65 gm of caffeine.

Caffeine, a xanthine alkaloid, mainly stimulates the cerebral cortex, the thalamus, the vasomotor and respiratory centers, and evidently the thermal regulatory mechanism. It reduces the cerebral blood flow. Among the acute and chronic toxic effects are insomnia, irritability, cardiac palpitation, tremor, convulsions, flushing, anorexia, dehydration from diuresis, fever, albuminuria, and epigastric discomfort. Seven of these features concerned my patient. The reflexes were not exaggerated, she had no tremor nor polyuria, but her habitual intake of phenobarbital and nicotine may have modified the action of caffeine. Moreover, her mildly psychoneurotic state may have played a role in her physical reactions. Variations in response also depend on whether a single large dose or repeated small doses are taken over a long period of time. Anyway, the nature and degree of reactions to caffeine are influenced by the age, the emotional or nervous state, or by the idiosyncrasies of people. Its action on physiologic functions is inconstant and variable, often diametrically opposite in different persons and even in the same person at different times.

Caffeinism is said to be current among intellectual workers, actresses, waitresses, nocturnal employees, and long-distance automobile drivers. Illness otherwise unexplained may be caused by excessive ingestion of the xanthine alkaloids, including those in coffee, tea, cocoa, and those in some popular beverages.

Generic and Trade Names of Drug

Phenobarbital—*Luminal.*

(The omitted figure and references may be seen in the original article.)

TREATMENT AND PROPHYLAXIS OF STREPTOCOCCAL INFECTIONS

For the past several years the Food and Drug Administration has been concerned regarding the efficacy of sulfonamides in the *treatment* of acute Group A beta hemolytic streptococcal infections. This concern has been shared by the American Heart Association which has been in correspondence with the Commissioner of Food and Drugs regarding advertising concerning the use of sulfonamides in the *treatment* of these infections.

Although earlier literature was unclear, more recent studies have established that sulfadiazine is not efficacious either in eradication of Group A beta hemolytic streptococci or in prevention of initial attacks of rheumatic fever. At the meeting of the Executive Committee of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association on April 14, 1967, the members again reviewed the use of certain sulfonamides and agreed that none of the reported studies has shown convincing evidence that the *treatment* of streptococcal infections with any of the sulfonamides will prevent the subsequent occurrence of rheumatic fever. On the other hand, both the Committee and the Food and Drug Administration recognize the efficacy of the sulfonamides in the *prophylaxis* of streptococcal infections.

The Drug Efficacy Review Panels of the National Academy of Sciences are currently reviewing claims of efficacy for all sulfonamides marketed during the 1938-1962 period. Official action of the FDA to modify claims for sulfonamides will be delayed until receipt of the formal recommendations of the National Academy of Sciences panels. In this interim period the FDA wishes to call to your attention to the fact that existing labeling or advertising of the sulfonamides suggesting efficacy of these products in the *treatment* of Group A beta hemolytic streptococcal infections is subject to the criticism expressed by the American Heart Association.

For your information, a pamphlet entitled "Prevention of Rheumatic Fever" is available from local Heart Associations or the American Heart Association, 44 East 23rd Street, New York, New York, 10010, which outlines their expert recommendations for both the treatment and the prophylaxis of streptococcal infections.—DHEW, Food and Drug Administration, Washington, D.C.

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